

THE INFLUENCE OF CERTAIN ANTACIDS ON THE ACIDITY OF  
HUMAN GASTRIC JUICE, WITH ESPECIAL REFERENCE TO  
MAGNESIUM TRISILICATE.

by

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"Don't think - try; be patient, be accurate".

John Hunter.

"Be not the first by whom the new is tried  
Nor yet the last to lay the old aside".

Pope.



## PREFACE.

At the present time "The Alkalies" are certainly amongst the most frequently prescribed of drugs, but, on the other hand, it is equally true to say that numerous authorities proscribe their use almost entirely. While clinicians of experience denounce Sodium Bicarbonate as "the Opium of the stomach," pharmacologists continue to investigate and recommend new antacids. The use of antacid drugs in the treatment of peptic ulceration is of minor importance when compared with rest in bed, and dietetic treatment, yet, modern research, emphasising as it does the importance of "free" acidity in the production and persistence of this lesion, would seem to justify one in assuming that healing might be expedited during the initial stages of treatment by adequate exhibition of the most suitable remedy. At all events, since most physicians continue to prescribe these preparations in large quantities, it is desirable that information should be available regarding their comparative efficacy in the human subject. This investigation is an attempt to amplify such knowledge as we already possess, and especially to observe over a prolonged period the effects of various antacids under conditions such as obtain during a strict therapeutic régime. In this manner the following antacids have been investigated:- Milk, Sippy Powders No. I. and No. 2. (modified), Magnesium Trisilicate, Aluminium Hydroxide, and Tribasic Magnesium Phosphate.

It is with the greatest pleasure that I thank the many others who have helped me with this investigation.

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CHAPTER I.

SOME HISTORICAL NOTES ON ANTACID REMEDIES.

"Those about to study Medicine, and the younger Physicians should light their Torches at the fires of the Ancients."

Rokitansky.

The use of substances, which might now be classed as antacids, may be said to be as old as the Art of Medicine itself. Remedies of this nature for "indigestion" are found in the most ancient medical literature, and those early physicians probably derived their knowledge from their own folk-lore. In Western Medicine, except for the period dominated by Galen's teaching, these substances, in one form or another, would appear to have been continually in use for the treatment of digestive disorders right down to the present day.

In the beginning, and for long afterwards, remedies consisted of substances derived from animal and natural sources, such as powdered bones, shells, coral and chalk. A reference to these may be found in "Papyros Ebers" (C. 1500 B.C.) and there is a remedy from that source, probably from 3500 to 5000 years/



c.5000 - 1500 B.C.

years old:-

"Another remedy for indigestion.

A hog's tooth.

Crush to powder, put aside four sugar cakes, and eat for four days."

A more excellent combination of antacids than the carbonates and phosphates of calcium and magnesium can scarcely be imagined! This early pharmacologist, however, was doubtless mostly impressed by the extraordinary powers of mastication and digestion of the hog, and hoped to transfer these in some measure to his patient. Nevertheless, it is a remarkable coincidence, and perhaps the first example in Medicine of being "right, but for the wrong reason."

"Natron", which is a mixture of sodium carbonate, sodium sulphate and sodium chloride, is frequently mentioned in "Papyros Ebers", but, so far as the writer is aware, is not definitely prescribed for digestive disorders.

(as does Partington, 1937,)

Professor Dilling states that the "Nitre" of the Bible is probably the same as "Natron". But, even with the aid of a willing imagination, one has been unable to find any reference to "Nitre" which might justify the conclusion that it was used as a gastric antacid. (Bible (2)) Still, it is of some consolation to/

to reflect that they were at least vaguely aware of its acid-antagonistic properties, for Solomon wrote: "As he that taketh away a garment in cold weather, and as vinegar upon nitre, so is he that singeth songs to an heavy heart." (Bible (1) Proverbs 25.(v. 20))

In Greek medical literature little attention is bestowed upon antacids. Alston (1770), who deals fully with these drugs, states that he could find no reference to them in the writings attributed to Hippocrates (C. 420 B.C.). Mutch ((1), 1936) however, states that Dioscorides (A.D.170) mentions the use of silicates, now regarded by many as the latest addition to the bewildering host of antacid remedies available to a puzzled profession and credulous public.

At the beginning of the Christian Era Celsus (A.D. 25) omitted all mention of such substances, prescribing a dietetic regime only in gastric disorder, but Pliny (C.A.D. 77) wrote enthusiastically regarding the virtues of coral, which, "calcined, pulverized and taken in water gives relief to patients suffering from griping pains in the bowels." He issued a word of warning, too, against excessive and prolonged exhibition of the preparation, for, he said, "if this medicament is frequently taken internally, the spleen will gradually be consumed." No references however were found in the works of Galen (C.180 A.D.),  
or/

or in the eight volumes of Paulus Aegineta (C.725 A.D.). And so into the darkness of the barren Middle Ages, when, for centuries, Galen was the supreme authority, and the progress of Medicine paused for a time.

The oldest dispensatory in the Library of the Royal College of Physicians, Edinburgh, that of Nicolao (1505) contained, so far as the writer was able to discover, no relevant material, but Professor Dilling mentioned an historical reference in the English Dispensatory of R. James (1764, 3rd Ed.), which unfortunately the present writer could not consult, which gave a clue to earlier uses of the remedies under discussion. James, discussing "Absorbents," stated: "But they were sparingly used by the Ancients and only brought into credit by Belmont and Tachenius, and their two followers in Holland, Sylvius (probably 1478-1555) and Bontekoe, who assigned an acid as the cause of many diseases, and prescribed absorbents for their cure." Also Schroeder (1659 iv.1.) stated that Paracelsus (1493-1541) prescribed pearls for stomach disorders. He, ~~also~~ in his "Complete Chymical Dispensatory" (1659), made frequent reference to the use of "absorbents" in stomach disorders. It would appear therefore that by this time their efficacy was securely established in England. On page fifty-eight he referred to Rhasis (the Arabian physician/



1659 - 1718 A.D.

physician Rhazes A.D. 850-932) who was reported to state that "shoe-soles burnt are excellent against the pains of the cholick." (One wonders if this effect could possibly be attributed to the adsorbent properties of powdered charcoal, - but such imaginative flights must be restrained!) Schroeder also mentioned "Bones, Crusts, Shells, Horns," and particularly stressed the efficacy of "the tooth of an Elephant, Boar or Wolf," "the Ankle-bone of a Hare," and, quaintly, "the Bone in the Hart's Heart," which make excellent medicine against Cholick." On page 153, he made the important statement concerning Chalk, that "it is sometimes given inwardly in the burning of the stomach called Heart-burn." Corals (p. 161) and Pearls (p. 167) are also commended for stomach disease, especially as elegant prescriptions for wealthy dyspeptics. He maintains that Paracelsus (1493-1541 A.D.) recognised the value of Pearls, prescribing them for many conditions including affections of the stomach. Finally, on page 175 he concludes that Marble, Serpentine and many similar substances help the Cholick, or Gripings and Belly-ache."

And so we pass from the fifteenth, sixteenth and seventeenth centuries to the eighteenth, when medical literature soon becomes more abundant. Quincy (1718) in "A Compleat English Dispensatory" deals fully with "absorbents/

1718 - 1777.

"absorbents". "Crabs-claws" were prescribed in Gas-coigne's Powder"; "wonderful virtues" were still ascribed to pearls, "but concerning these Quincy was sceptical; nevertheless, he says, physicians "may secure their retreat in having done no harm." Of Chalk he writes that "its most experienced Virtue is in removing that Uneasiness at Stomach, which is commonly called the Heart-burn," while concerning Red Coral, that it is "accounted a great sweetener, and therefore prescribed with good reason to correct the acidity in the Stomachs of young Children."

Towards the mid-eighteenth century one finds Boerhaave (1738) writing of Absorbents of Acids, and quoting such substances as Chalk, Bole, Bonebinder, Marl, Corals, Pearls, Mother of Pearl, Limpin Shells, Oyster Shells, Claws and Shells of Crabs, Lobsters, dried fish bones, and the "Jaw Bone of a Jack." He also deals with Immutants of Acids i.e. alkaline salts fixed from combustible vegetables. Alston (1770) discusses at considerable length the various antacids in use in his time, mentioning particularly oyster shells, chalk, coral, and pearls. James (1764) refers, as noted above, to the history of "absorbents", and mentions, in addition to the above, powdered egg shells. In 1777 one finds Black cautiously advocating Magnesia Alba as a purgative and absorbent earth.

The/

The German physician Hoffmann is his authority, and Black writes "that although Magnesia appears from this history to be a very innocent medicine, yet having observed that some hypochondriacs who used it frequently were subject to flatulences and spasms, he, (Hoffmann) seems to have suspected it for some noxious quality. The circumstances however, which gave rise to his suspicion may very possibly have proceeded from the imprudence of his patients, who, trusting too much to Magnesia (which is properly a palliative in that disease) and neglecting the assistance of other remedies, allowed their disorders to increase upon them... But there seems at least no objection to its use when children are troubled with too much acid in their stomach." Other dispensatories and allied works at this time reiterate what has already been said without adding new material or interesting amplification concerning what has already been written.

At the opening of the nineteenth century Rotherham's "Dispensatory" (6th Ed. 1801) and Gregory's "Conspectus Medicinæ Theoreticæ" (1803) were published but contained little of special interest.

However, Duncan's "New Dispensatory" (11th Ed. 1826) contains some interesting material, especially with regard to magnesia and chalk. "Carbonate of Magnesia" (he writes p. 595) "is principally given to correct acidity/

acidity of the stomach, and, in these cases to act as a purgative .... whereas, carbonate of lime, in the same circumstances binds the belly." He thus anticipates the principle emphasised in the Sippy régime for the treatment of peptic ulcer.

Duncan also points out that magnesium carbonate often gives rise to flatulence due to the production within the stomach of carbonic acid gas, and suggests exhibiting "magnesia" ( $MgO$ ) where this proves troublesome; but where there is nausea and vomiting he considers that benefit may accrue from the activity of the gas evolved. Discussing the antacid qualities of chalk (p.588) he refers to its use where diarrhoea is also present, and remarks that "the fear of its forming concretions in the bowels is probably imaginary; for it is not warranted either by theory or experience." This fear has not yet been completely allayed!

So far physicians (with the possible exception of Celsus) have concerned themselves only with drugs and "remedies" in their endeavour to deal with excessive acidity, but about the period now reached, food itself, and, in particular, milk, begin to be recognised as important, and much more "physiological", controllers of the acidity of the gastric juice: indeed, leading physicians about this time were as alarmed by the excess and abuse of alkali treatment as their fellows have been almost a century later!

According/

According to Ziemssen (1877), Cruveilhier was the first to suggest milk as a combined food and ant-acid in 1832, and he endeavoured to prevent a long continued collection of acid in the stomach by administering frequent small milk feeds.

In 1846 an article by Trousseau abstracted from "Le Journal de Medicine" appeared in the first volume of "The Lancet" (p. 318) "On the abuse of alkaline preparations". In it he asserts that "it cannot be a matter of indifference to neutralize the acids which the economy wants... The digestion of amylaceous substances becomes therefore incomplete or extra natural.... If taken in large quantities, they occasion a cachetic condition followed by a deplorable state of emaciation. The ancients before us had remarked that at last a cachexia became established characterised by paleness, general puffiness of the tissues and passive haemorrhage." This latter of course does not conform to the modern conception of "alkalosis", and the manifestations described were probably due to the progress of the original disease, perhaps an advanced renal, hepatic or cardiac condition. Trousseau concludes by exhorting clinicians to "assist nature"; "how is it," he writes, "that physicians do not see that a remedy powerful to cure is also powerful to do evil. Alkaline remedies are daily administered/



1846 - 1877 .

administered with inconceivable indifference." Few would deny that these remarks continue to apply in some measure to this day. Apart from the rare "alkalosis", all too often, "baking soda", and its more elegant relatives, are "prescribed", (frequently by the patient himself) for "indigestion pains", which pain, having been relieved, the real malady remains uninvestigated and untreated till some disaster such as haemorrhage or perforation occurs. A clinician of considerable experience known by the writer is wont to declare, (with dramatic exaggeration), that sodium bicarbonate is one of the really "dangerous drugs" still unembraced by "The Act."!

In the latter half of the nineteenth century modern methods of treatment of disorders of digestion are gradually adopted. Chambers (1856) in his book dealing with this subject recommends alkaline small milk diets, with frequent small feeds and powdered chalk after meals. If there is pain he gives alkalis, but states they are "anodynes and don't neutralize the acid".

In his "Cyclopaedia of the Practice of Medicine" Ziemssen (1877) wrote that alkaline mineral waters containing sodium carbonate had two actions:-

- (1) "they neutralize the excess of acid
- (2) they excite the diseased mucous membrane to secrete gastric juice,"

that this had been confirmed by experiments with gastric/

1877 - 1889.

gastric fistulae in dogs, and that therefore they should be used in the "atonic forms of gastric catarrh". He suggested giving moderate doses of antacids for "heart-burn and acid eructations", but issued a warning against excessive or prolonged administration of these drugs.

In 1889 Sir William Roberts stated that the gastric antacids in common use "consist of the alkaline and earthy carbonates and lime water," and there is little to choose between them. "The alkaline bicarbonate" however "has a nauseous taste, and taken in excess leaves an alkaline residuum in the stomach. This is at least abnormal and perhaps embarrassing in an organ which requires the presence of acid to perform its functions. Earthy carbonates are tasteless and owing to insolubility cannot cause neutral line to be over-passed." He did not believe that any harm would result from prolonged carefully regulated use of these drugs. He also provided the first table of antacid equivalents the writer has discovered from the results of experiments in vitro. He found that

10 grs. sodium bicarbonate	= 12 grs. pot. bicarb.
	= 6 grs. creta precipit.
	= 6 grs. carb. magnesia.
	= 3 grs. calcined magnesia.
	= 6 fl. oz. lime water.
	= 2 fl.drachms liq.potassae.
	= 1 bismuth lozenge B.P.

10 grs. sodium bicarbonate =  $2\frac{1}{2}$  Wyeth's soda-mint tablets.

= 5 Vichy Lozenges.

Towards the end of the 19th century physiologists, pharmacologists and clinicians began to apply the experimental method of study to the problems of the antacids' effects and a considerable amount of work was done both by way of laboratory and clinical research. The results however were conflicting. Discussion of this work really falls within the scope of the next chapter, and will be dealt with briefly there.

This, then, concludes an outline of the history of antacid therapy. Although one has perhaps laid more emphasis on the "antacid" nature of early remedies than their authors could have intended, yet, it may at least be said that certain interesting coincidences occurred in the Literature of the Ancients, and it seems certain that many of the remedies mentioned at the beginning of this chapter were administered, on occasion, to cases requiring "antacid" therapy. One has been especially interested to find that it is almost one hundred years since "alkalosis" was first discussed, and even longer since milk was advocated as an antacid of the first importance, while the method of controlling the action of the bowels by suitable combinations of the antacids, (recently emphasised by B.W. Sippy, (1915)), was being taught in the Edinburgh School by Duncan in the early



years of the nineteenth century.

### SUMMARY.

Notes on antacid remedies have been collected from medical literature throughout the ages beginning with the "Papyrus Ebers" and continuing with references from the literature of the Greeks and Romans to the "dispensatories" of the sixteenth, seventeenth, and eighteenth centuries. The use of these remedies for stomach troubles" can be traced (with the aid of a little imagination at times) from the earliest times right down to the present day.

It has been especially interesting to note that it is over a hundred years since the principle of controlling the bowels by means of variations in the antacids given for "heartburn" and allied conditions was first taught in the Edinburgh School, and almost as long since milk was first advocated as an antacid of the greatest importance.

[illegible]

CHAPTER II.THE ANTACIDS.A REVIEW OF THE LITERATURE.I. Experimental work prior to the introduction of the fractional test meal.

It was stated at the end of the last chapter, that certain physicians and others, towards the end of the nineteenth century, began to question the simple faith of their colleagues in the reported but unproved effects of alkalis on gastric secretion, and numerous experiments in vitro, on animals, and on patients, were carried out in an endeavour to determine in a scientific manner the true nature of their action. This work was excellently epitomised by B.B. Crohn (1918). Opinions resulting from this early work were most conflicting, for laboratory workers and clinicians, physicians and physiologists disagreed not only with one another, but also amongst themselves. For example, Bickel (1905), and Heinsheimer (1906) in the laboratory concluded that alkalis, such as sodium bicarbonate, led to a gastric catarrh and diminution in acid secretion, whilst at the bedside, using the method of successive test meals, von Leube (1874), du Mesnil (1892) and Linoissier and Lemoine (1894) were equally convinced that the result of alkali medication was immediate or ultimate increase in acidity. On the other hand, Mathieu/

Mathieu and Laboulais (1894), using the same clinical method, found diminution of acidity both immediately after alkali administration and after prolonged use, while the famous physiologist, Claude Bernard, as early as 1879 had noted, from his laboratory, that "le suc gastrique s'écoule en plus grande abondance quand on introduit des alcalines dans l'estomac".

Probably the most important and careful experimental work of this period was that of Pawlow and his co-workers, carried out during the last years of the century, and published in his classical work on the physiology of digestion (2nd Ed., 1910). In these investigations, dogs with oesophageal fistulae and "Pawlow Pouches" were used, and were fed on meat with the addition of sodium bicarbonate. He found (p.95) that "to sodium bicarbonate an inhibitory influence must be ascribed; not one of the soda solutions .... were able to expel a single drop of juice from the small cavity" (Pawlow Pouch). On page 145 he discussed the therapeutic applications of his results and noted that "it is stated now as ever in text-books that these substances (alkalis) promote a flow of gastric juice. We may look in vain, however, for any experimental foundation to support this doctrine. The experiments brought forward cannot be regarded as conclusive since, naturally, the stomach under the influence/

influence of alkalis, sometimes began to secrete a greater quantity of gastric juice. This means, however, that it has recovered from a disordered state, and has returned to normal conditions". He found the salivary, gastric, and pancreatic glands were all affected, and that the healing effects of alkalis were due to their giving "rest to the gastric glands". He believed that the cause of "previous error" had been that workers had omitted consideration of the effects of saliva and the stimulant effect of the water in which the drugs were administered. Immediate protests were forthcoming from observant clinicians who endeavoured, by the method of successive test meals, to establish their claims regarding the succagogue effects of sodium bicarbonate; but the method was far from satisfactory, results were again conflicting, and Pawlow's views were accepted by most physicians for many years.

The introduction of the fractional method of gastric contents' analysis by Rehfuss (1914), however, provided a new and better method for the study of the effects of drugs on the human stomach's secretions, and it was soon adopted by workers all over the world. The literature relating to this small subject is now immense, and papers have been published from Alaska to New Zealand, from Japan and China in the far East to Kansas City in the "Middle West". Thus it has not/

not been possible to consult every article in this literature, but it is hoped that no work of importance directly bearing on the present investigation has been omitted.

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The Actions of antacids in vitro.

Before going on to discuss the more recent clinical research which followed the introduction of the fractional test meal, the various investigations into the antacids' effects in vitro will be reviewed.

Roberts' (1889) table of antacid equivalents has already been given (p.11) and it will be remembered that he estimated that calcium carbonate and magnesium carbonate were almost twice as powerful as sodium bicarbonate, and that magnesium oxide had over three times its acid neutralising power.

After "alkalosis" cases had been reported by Hardt and Rivers (1917), and the unsatisfactory nature of these remedies had been demonstrated by Crohn et alia (1918) a search was instituted for the "ideal" antacid. The properties of an "ideal antacid" according to Loevenhart and Crandall (1927) are as follows. It should:-

be insoluble and incapable of absorption from the alimentary tract,

not have an irritant action on the alimentary tract,

be neutral in aqueous suspension, but be capable to neutralising acid:

not cause urine to become alkaline (with danger of stone production from phosphate precipitation) when taken in reasonable amounts,

not cause diarrhoea or constipation:

not cause serious alteration in mineral metabolism.

1923 Greenwald suggested the di- and tri-basic phosphates of calcium and magnesium, coming to the conclusion that tribasic magnesium phosphate was probably the best, since, in vitro, it neutralised  $\frac{N}{10}$  hydrochloric acid well, could not produce an alkaline reaction, nor liberate carbon dioxide (see also p. 39). This subject was much more fully investigated by Freezer et alia (1928) who came to the conclusion that tribasic magnesium phosphate was apparently the most suitable and bismuth oxycarbonate the least effective antacid in their series. They found milk to be active in acid neutralisation, and questioned whether it was not the most important factor in alkaline therapeutics. They summarised their results in the following tables which show the relative efficiencies of the various antacids tested:-

Antacid	Amount of antacid required to neut- ralise 100 c.c. 0.3% HCl	Relative antacid efficiencies. (Sodium Bicarbonate = 100%)
	100 c.c.	-
um Bicarbonate	0.61 gm.	100%
ium Carbonate	3.36 gm.	20%
esium "	0.47 gm.	145%
esium Oxide	0.214 gm.	317%
esium Peroxide	0.42 gm.	160%
asic Calcium hosphate	1.10 gm.	61%
asic Magnesium hosphate	1.31 gm.	51%
otassium Citrate	1.17 gm.	58%
odium Citrate	1.10 gm.	61%
uth Oxycarbonate	-	0

Filinski (1929) found the following amounts of antacid neutralised  
c.c. of  $\frac{N}{10}$  Hydrochloric Acid.

Magnesium Oxide	=	2 gm.
Magnesium Peroxide	=	5.6 gm.
Sodium Bicarbonate	=	8.4 gm.
Aluminium Silicate	=	2.5 gm.
$(Al_2 Si_6 O_{15}, 2H_2O)$		



Clark (1937) also provides a few antacid equivalents as follows:-

Amount of antacid required to neutralise  
1500 c.c. of gastric juice of acidity  
equivalent to 0.3% Hydrochloric Acid.

(Estimated amount secreted by stomach in 24 hours).

Magnesium Oxide	3 gm.
Sodium Bicarbonate	12 gm.
Magnesium Carbonate	7 gm.
Calcium Carbonate	7 gm.
Bismuth Oxycarbonate	136 gm.

He advocates that magnesium oxide be given since it is most efficient, and occurs no liberation of carbon dioxide, which stimulates further acid secretion. Cushny (iii) (1936) merely quotes Clark's investigation. It will be noted that Clark's results differ markedly in the case of magnesium and calcium carbonate from the findings of Freezer et alia.

With regard to the most recently introduced antacids, the following results have been collected from the literature:-

(a) Aluminium Silicate ( $\text{Al}_2 \text{Si}_6 \text{O}_{15}, 2\text{H}_2\text{O}$ )  
2.5 gm. = 100 c.c.  $\text{N}/10 \text{ HCl}$  (Filinski, 1929)

It is therefore almost as effective as Magnesium Oxide (2 gm.). ( This would be equivalent to 254% in Freezer's Table).

(b) Calcium silicate.

1 gm. = 57 c.c.  $\frac{N}{10}$  HCl (E. Becker, 1933)

(Mahler (1934), however, states that magnesium oxide is seven times more powerful in vitro).

Equivalent thus to 363% sodium bicarbonate in Freezer's table).

(c) Magnesium trisilicate.

1 gm. = 310 c.c.  $\frac{N}{20}$  HCl. (Mutch, 1936).

(He states that with acid of this strength, 75-80% of the antacid is neutralised almost immediately, i.e. within the first few hours).

Equivalent thus to 951% sodium bicarbonate in Freezer's table.

(d) Aluminium hydroxide.

1 gm. = 40-50  $\frac{N}{10}$  HCl (approximately).

Ivy et alia (1937) found that 4 c.c. "Alucol" (which is 55% suspension of aluminium hydroxide) neutralises 40 c.c.  $\frac{N}{10}$  HCl in a test tube.

Einsel et alia (1934) state that a good suspension of aluminium hydroxide should neutralise at least 100 c.c.  $\frac{N}{10}$  HCl per 4 c.c. and thus the figure 40-50 c.c. per gram for the pure drug is obtained; this would be 30% sodium bicarbonate in Freezer's table.

The various test-tube results therefore have been found to vary considerably.

The writer's results were as follows:-

One drachm Sippy Powder No.1	=	774 c.c.	<sup>N/</sup> 10 HCl
One " " " No.2	=	531 c.c.	" "
One " Tribasic Magnesium Phosphate	=	480 c.c.	" "
One " Magnesium Trisilicate	=	171 cc.	" "
		(in 60 minutes)	
	=	120 c.c.	" "
		(in 30 minutes)	
One " Aluminium Hydroxide	=	66 c.c.	" "
		(in 30 minutes)	

These powders were chosen since they are the ones employed in this investigation. The fact that pure sodium bicarbonate was not used makes comparison with the results of others a little unsatisfactory. While the first three results might have been expected from Freezer's investigation, the last two appear to be considerably less effective than Mutch and Einsel's results would have suggested. It will later be shown that these results bear little relation to their comparative efficiency in vivo.

Experimental work and literature since the  
introduction of the fractional test meal (1914).

At first experiments were concerned with the alkalis, such as sodium bicarbonate and sodium citrate, and also other antacids such as calcium carbonate and magnesium oxide, but, when these were found to be on the whole unsatisfactory, research was directed towards the discovery of the "ideal" antacid. Many substances have been suggested, but only those used in this investigation, namely, milk, Sippy Powders No.1 and No.2 (modified) and their constituents, magnesium trisilicate, tribasic magnesium phosphate, and aluminium hydroxide, will be discussed in detail; others, such as atropin, histidine, and "gastric mucin" may be dealt with briefly or omitted altogether as their importance seems to indicate.

It was Crohn (1918) who first used the above method. He was surprised and disappointed by his findings, and since then many have been chary of using "the alkalis" at all. He investigated numerous antacid agents, giving them at various periods before and after the ingestion of a gruel test meal and compared the responses with his controls. He did not mention how many cases were investigated, but gave the impression that the results shown were characteristic/

characteristic of a large series. He concluded that with small doses of alkalis (e.g. gr.xx sodium bicarbonate) no beneficial neutralisation occurred, whilst a secondary acid response, often higher than the control, resulted. With larger doses, neutralisation occurred, but peptic digestion was paralysed for a time, this being followed by a very high secondary acid response. This was especially marked in the cases of magnesium oxide, hydroxide, and carbonate, which were three and a half times as strong as antacids as sodium bicarbonate. Bismuth subcarbonate, he found, was only 36% as powerful as sodium bicarbonate but its breakdown to bismuth oxychloride was slow, and therefore a gradual and prolonged antacid action occurred without the production of a secondary secretion. Olive oil, and atropin by mouth and hypodermically were disappointing except in cases of hypersecretion. He suggested that small fractional doses of magnesium oxide ("the most dependable") in combination with bismuth subcarbonate (for its prolonged action) would be the most "physiological" method of administering such medicaments, but concluded that prolonged use, far from causing a permanent diminution of acid secretion, probably caused the reverse effect.

Finally, he pointed out that lasting relief was not to be expected from any antacid therapy, but rather/



rather was it to be sought in the study of the general manner of living of the patient, and the correction of hygienic and dietetic errors. (The "antacid effectiveness" of the Sippy regime for the initial healing stage of peptic ulcer (B.W. Sippy, 1915) was not investigated by Crohn.

Bennett (1922) similarly investigated the action of certain drugs on gastric secretion and motility and came to the following conclusions:-

(1) Substance diminishing gastric secretion.

Atropin was found to be a depressant of gastric secretion "as powerful as when applied to the eye", especially when used in weak solution, on an empty stomach.

(This is at variance with Crohn's findings just quoted).

(2) Substances affecting secretion after its evolution.

(a) Sodium bicarbonate excites a secondary secretion which more than counter-balances its neutralising effects (as with Crohn).

(b) and (c) Magnesium hydroxide and bismuth carbonate were less stimulating, and had stronger neutralising effects.

He recommended that all such drugs be given after food (as did Crohn, (1918)), and that for arresting secretion, atropin was much the most effective substance. More precise data were not provided in this short article.

Next came the work of Lockwood and Chamberlain (1923) who investigated, by means of the Ewald Test Meal, the effect of four antacids on the same patient, within a week, 26 tests being carried out in all. Sodium bicarbonate, (8 tests) calcium carbonate (6 tests) magnesium oxide (5 tests) and bismuth sub-nitrate (7 tests) were used.

- (1) Sodium bicarbonate (4 gm.) average "free" and total acidity was higher on less than 25% of cases, but at some point acidity was higher than control in 50% of cases.
- (2) Calcium carbonate (4 grams) and magnesium oxide (2 grams) resulted in lower average "free" and total acidity in all cases; controls' results were exceeded at some point in 25% of former's and 20% of latter's cases.
- (3) Average acidity was unaffected by bismuth sub-nitrate, but in 2 out of 7 cases control was again exceeded.

The effect on stomach evacuation or biliary regurgitation was not noted in any case.

Although the results of this investigation are apparently fairly satisfactory, one notes that only a small series of cases (5 to 8) were investigated for each drug, and the Ewald type of test meal was used, which/

which provides much less precise information regarding the course of secretory activity than the fractional method of Rehfuess; moreover, the precise extent and duration of acidity control was not indicated.

About this time, as a result of the above findings, and the reports of Hardt and Rivers (1923) and Binger et al (1923) on the toxic action of therapeutic doses of sodium bicarbonate, a search was instituted to discover an "ideal" antacid, (see also p. 18 ). Greenwald (1923) imagined this "ideal" substance to be one which:-

- (1) could not make the stomach contents alkaline and produce a secondary hyper-acidity, and
- (2) would be excreted unchanged from the intestines.

He therefore suggested that the secondary and tertiary phosphates of calcium and magnesium be used, and demonstrated how, when titrated with  $\frac{N}{10}$  Hydrochloric acid, they neutralised the acid, and this without the production of an alkaline reaction when present in excess. He considered them better than calcium carbonate because no belching was produced, than magnesium oxide, because this could produce an alkaline reaction with pH 9 in the solution, and than/



than bismuth subcarbonate, because of its poor neutralising potentialities. Kantor (1923) used these "neutral antacids" clinically on 220 patients and claimed excellent results. He considered that the tribasic phosphates were the strongest antacids ( $Mg_3(PO_4)_2$ , and  $Ca_3(PO_4)_2$ ), the magnesium salt being slightly laxative, while the calcium salt had the opposite effect; they were tasteless, had no demonstrable effect on the economy and were not excreted in the urine. Although less powerful than sodium bicarbonate and magnesium oxide, they could be given in larger doses (1 to 6 grams) over prolonged periods without danger of alkalosis. He included only one test meal result in his paper, 3 grams of the antacid being given one hour after the meal. The effect of this, though described as satisfactory, was by no means dramatic, the acidity never being completely neutralised, and a considerable secondary acid secretion following such antacid effect as had occurred.

In 1922 Roch (1922) had introduced aluminium hydroxide as an effective neutral antacid. Work relating to this substance, and to magnesium trisilicate is reviewed separately at the end of this chapter.

But these "ideal" antacids, (theoretically at least),/

least), were not generally adopted, and workers continued investigations on sodium bicarbonate calcium carbonate and the rest. Boyd (1925) (i) found that in dogs, with "Heidenhain" Pouches, sodium bicarbonate in doses up to 1 gram per kilo body weight neither reduced permanently the acidity nor the quantity of the gastric juice, and often produced gastro-intestinal irritation. When calcium carbonate was added to control the diarrhoea, depression of acidity did not occur till 3 grams per kilo body weight of the mixture was given. There was then evidence of considerable diminution of the blood chlorides which might account for the depression of gastric acidity. So soon as antacids were stopped, a hypersecretion resulted lasting several days. Continuing his investigations on human subjects, Boyd (1925)(ii) found that sodium bicarbonate up to 1 gram per kilo body weight caused no lasting depression of gastric secretion; with small doses the secretion was above normal, with larger doses there was a decrease in quantity and acidity of secretion. When given after feeding, a larger dose was required than when given with water alone. Calcium carbonate alone led to an increased flow of gastric juice whether given on an empty or digesting stomach. Shortly after this, however, one finds Keefer and Bloomfield (1926) and Loevenhart and Crandall (1927) writing/

writing in favour of these very substances. The former workers investigated by means of the test meal method, the effect of sodium bicarbonate on 12 cases. They stated that 1 gram of sodium bicarbonate would neutralise 75 c.c. <sup>N/10</sup> Hydrochloric Acid (Freezer (1928) found that 0.61 gram would neutralise 100 c.c. <sup>N/10</sup> HCl), and that, with this dose, the stomach would empty before an acid secretion could be re-established unless "a great deal of acid is being secreted!" Furthermore, their conclusions were at variance with those of nearly all other workers in this field, for they found that the introduction of alkali into the stomach caused neither an increase nor a decrease in the volume of gastric juice secreted, and that the time of re-appearance of "free" acid in the stomach after giving sodium bicarbonate depends largely on the emptying time and motility, the volume of secretion being of less importance. They found no change in motility and "no evidence that this alkali occasioned effects other than the quantitative neutralisation of gastric acid". These results stand practically alone in the literature consulted, and must be due to some difference in technique not fully described by the authors. Loevenhart and Crandall, while advocating calcium carbonate, condemned sodium bicarbonate, magnesium carbonate and magnesium hydroxide because:-

- (1) the relief from pain was quite temporary.
- (2) they irritated the intestine on the concentrations usually employed leading to "irritable colon",
- (3) being soluble, it was impossible to regulate the concentration on the stomach,
- (4) in excess, alteration in blood chemistry and urinary reaction was produced with possible precipitation of phosphatic calculi, and also the production of alkalosis.

Nor were they impressed by bismuth subcarbonate or subnitrate which were "inert insoluble powders", which caused black stools and only alarmed the patient. But calcium carbonate (the first antacid known to man!), - here was the "ideal antacid", for was it not (i) bland, (ii) insoluble, but a "potential alkali", (iii) without effect on the bowel, (iv) a minimal disturber of acid base equilibrium and mineral metabolism, and (v) "fool proof" in the hands of patients. It should be prescribed (they said) as tablets with the addition of a small amount of some carminative. Most writers are of opinion, however, that carbon dioxide is liberated in undesirable quantities, and, apart from causing distension may be responsible/

responsible for a stimulation of acid secretion: moreover, a constipating action is often attributed to it. This paper was unsupported by any experimental work, and the conclusions would appear to exaggerate the virtues of calcium carbonate as Boyd (1925) and other authorities found them.

Paulsen and Sternberg, (1927), investigated the effect of three antacids on the same patient following a bouillon test meal. They publish charts of only two cases, "essential" hyperacidity and "gastric ulcer", and conclude that sodium bicarbonate, and to a slightly less extent, magnesia produce an excessive alkalisation of the gastric contents followed by a marked secondary rise in acidity, whilst in both cases aluminium silicate ("Neutralon"), while producing an equally prolonged neutralising effect, appears to have neither of the above undesirable characteristics. (References to the action of silicates are collected and discussed separately at the end of this chapter, see page 46 ).

On the Continent at this time (Degener (1928) investigated magnesia's effect on the acid response to a test meal of 300 c.c. 5% alcohol, in 36 patients. He gave 2.5 grams 40-60 minutes after the meal, and found that it accelerated emptying, and neutralised the "free" acid for one hour or more in "normal" acidity/



acidity cases, and up to half an hour in hyperacidity cases).

Filinski (1929), again using alcohol test meals, investigated five antacids, and published the results of each of two patients, referring to an indefinite number of others, which showed similar results. He found the usual excessive alkalinising action of sodium bicarbonate (10 grams) and with others tested (magnesium oxide 4 grams, magnesium peroxide  $\text{Mg}_2\text{O}_2$ , 4 grams (25%), hydrogen peroxide  $\frac{1}{2}\%$ , and aluminium silicate,  $\text{Al}_2\text{Si}_6\text{O}_{15} \cdot \text{H}_2\text{O}$ ) he found hydrogen peroxide had the most prolonged effect, magnesium peroxide next, and aluminium silicate was least satisfactory by far. He emphasised especially the wide individual variation in each patient, (especially the increase in acid in the later secretion period), recommended the use of a combination of sodium bicarbonate and magnesium oxide frequently, since <sup>their</sup> effect is short, given half an hour after food as most suitable in practice. During healing of an ulcer, food should be taken hourly.

Mahler (1934) examined the influence of numerous antacids on two-hour alcohol test meal acid responses in the same patient, and found that in eight cases studied, magnesium carbonate and magnesium oxide gave the best results, sodium citrate came/

came next, while sodium bicarbonate's marked secondary acid stimulation at the end of the second hour led to its being placed fourth on the list. Magnesium ammonium phosphate and aluminium hydroxide (see also page 42 ) came last in the list! Calcium silicate was also investigated (2 cases) with favourable results (see page 47 ). He emphasises the importance, in comparing the effects of such drugs, of giving the same dose (in this case 5 gm.), and points out how results obtained in vitro may be quite misleading regarding the effects of drugs in vivo.

Becker (K.P. 1935) using the "test meal" method in 30 patients (studied in groups of 10) found no decrease in the average secretion or concentration of acid with either sodium bicarbonate, or magnesium peroxide, but obtained most favourable and lasting effects ~~with  $(MgO_2)$  but obtained most favourable and lasting effects~~ with aluminium silicate (see page 48 ).

Returning once more to American investigations, Wosika and Emery (1936,a) studied the effectiveness of the complete Sippy regime in neutralising the "free" acid in 17 cases. The tests lasted 12 hours (7 a.m. to 7 p.m.) and patients were during the first test given the milk and cream feeds without the powders. Their results (with powders added) showed:-

(1) that the "free" acidity was completely controlled in half the cases,

(2)/

- (2) that of the "free" acidity does not rise above 20 clinical <sup>units</sup> ~~visits~~ following the "alcohol test meal" (50 c.cs. 8% alcohol) - adequate control is achieved, but above this point there could be no certainty of the effect.
- (3) that only a relatively slight difference in "free" acidity was achieved by the addition of the powders to the milk and cream feeds, on the second day of the test.

This last observation seems of considerable importance since, if confirmed, it would fully justify the cessation of alkali therapy advocated by many.

The same workers (1936,b) carried out similar tests on ~~other~~ <sup>a smaller further</sup> 14 patients, using powdered milk (12.5 grams) given with the alkalis hourly, and found acid neutralisation somewhat more efficient, due, they suggested, to lessened "appetite" secretion. They actually advocated this form of treatment, quoting in further support of it that it is more easily administered, smaller curds are formed in the stomach, it is easier to carry about, and slightly less expensive.

It may be said at once that the writer would not consider adopting this "refinement" of therapy, but it is quoted merely as an extreme example of "antacid" enthusiasm.

(Wosika/

(Wosika and Emery state in this very paper that recent experiments have shown that complete acid neutralisation is by no means necessary for the healing of peptic ulcer!)

Finally, in this section dealing with the effects of the older antacids, mention may be made of a paper by Friedenwald and Morrison (1937) who review the present position of antacid therapy, and summarise the views of the leading authorities. They conclude that these remedies should certainly continue to be used, each patient being individually considered. They suggest that any of the antacids, even magnesium oxide and sodium bicarbonate, may be used without producing untoward effects (such as an excessively alkaline reaction or a secondary secretion) provided the correct dosage for the individual is prescribed. The determination of this correct amount, even if the patient's acid response to a test meal were to hand, would seem to the writer, after consideration of his own investigations and the results of others, to be well nigh impossible, and remedies with a wider margin of error than "the alkalis" are therefore to be preferred. The "neutral" antacids, such as tribasic magnesium phosphate aluminium hydroxide, mentioned by Friedenwald, thus commend themselves. The literature connected with those two remedies, and with that of the silicates, will now be discussed/

discussed separately, since it consists mainly of papers devoted exclusively to them, and since the study of their effects comprises an important section of this investigation.

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TRIBASIC MAGNESIUM PHOSPHATE.

As already noted, although this and allied substances have been used from ancient times, Greenwald (1923) in search of an "ideal" antacid first directed attention to their virtues as "neutral" antacids in vitro, while Kantor's clinical investigation (1923) supported Greenwald's claims. The tribasic magnesium salt was found to be best.

Clinical experience was apparently Kantor's chief criterion in assessing the value to the drug, for its effect on the acid response to a test meal was not dramatic in the only case published by him.

Friedenwald (1937) notes that Shattack et alia and Hurst recommend it for certain cases.

Mahler (1934) found magnesium aluminium phosphate inferior to magnesium carbonate, magnesium oxide, sodium bicarbonate and sodium citrate (see aluminium hydroxide page 40 ).

In vitro, the very satisfactory nature of this neutral antacid was emphasised by Freezer et al (1928).

In conclusion, therefore, it may be said that this remedy, theoretically and in vitro, should provide a most excellent means of neutralising gastric acidity, but little work in vivo has been carried out; such results as have been published have tended to support the claims made for this remedy.

### Aluminium Hydroxide:

Aluminium Hydroxide,  $\text{Al}(\text{OH})_3$ , was introduced by Koch (1922) but has received little attention in this country. Nevertheless it has been investigated frequently both on the Continent and in America.

Crohn (1928) first investigated this drug in America and found it superior to any other antacid so far discovered. He described it as a white insoluble neutral salt, prescribed as a permanent colloidal suspension, almost tasteless, and insoluble in water. He was dissatisfied with the soluble alkalis, especially sodium bicarbonate and also with magnesium oxide, magnesium phosphate, and even calcium phosphate, which either produced an excessive neutralisation and secondary secretion or else were poor antacids. He compared their effects on a gruel test meal acid response with that of aluminium hydroxide and found that, while it never produced an alkaline reaction, it was an efficient antacid which reduced the "free" acidity to the minimum consistent with continued gastric digestion; motility was hastened, while subjective relief was the invariable rule. He found it was non-absorbable and non-toxic. He did not state how many cases were thus investigated, but mentioned 50 cases successfully treated clinically.

Kreis (1931) reiterated Crohn's words regarding his clinical findings, and emphasised that a "jelly like"/

"like" substance is produced in vitro and in vivo which, he believed, lodged at the ulcer site and neutralised acid before it could reach the devitalised area. He also mentioned that acidity was never completely neutralised; the effect was gradual and prolonged (even to 4 to 5 hours), and no flatulence was produced. This worker estimated that it was between 10 and 20 times as efficient an antacid as the usual "alkali mixture", and was thus very economical. He published no precise results.

Einsel and Rowland (1932) treated 13 peptic ulcer patients with the remedy, claiming unusual success (gave 4 c.c. six times daily half an hour after food), especially in cases which had proved refractory to the usual alkalis. Vogl and Hillebrandt (1932) discussing this drug add nothing to the findings of Kreis; they, too, noted that  $\text{Cl}^1$  was combined with  $\text{Al}^1$ , and was excreted by the gut; this, they believed, tended to keep down gastric acidity.

Adams and others (1934)(1937), working from 1931 onwards, carried out a fuller investigation than any of the previous workers. They treated 110 patients with either gastric ulcer or hyperacidity and obtained poor results in <sup>only</sup> 9, and unimproved condition in 8 cases. Two-to three-hour alcohol test meals were given before and after treatment and it was found/

found that with colloidal aluminium hydroxide (4 c.c.) four times daily, "free" acidity never rose above 20 points, but with the same amount thrice daily it reached 30 points on two occasions at the end of the test. As treatment progressed, the acidity curve tended to progress to a lower level, due, they believed, to increased secretion of mucus and an astringent effect; but, on cessation of treatment, the former acid levels were again attained. They observed no toxic symptoms, even with large doses (e.g. 3 drachms six times daily for 3 weeks); slight constipation was treated with paraffin, etc. Continuing their investigation (1937) they found no increase in the aluminium in the blood, no significant change in the serum chlorides, carbon dioxide content, or total base in the blood; in fact the acid base equilibrium of the blood was unaltered after three months medication. They conclude from a review of the literature, subjective improvement of the patients, and the laboratory findings, that this is the most satisfactory antacid yet employed.

Mahler (1934), in his comparative study of the effects of antacids on two hour alcohol test meals on nine cases, concludes that aluminium hydroxide (5 grams) is less effective than magnesium oxide, magnesium carbonate, sodium bicarbonate on sodium citrate. This result is probably due to the large dose/

lose of antacid used, and the short duration of the test which does not permit the secondary hypersecretions time to manifest themselves fully.

Woldeman and Rowland (1935) had apparently no doubts as to the efficacy and innocuous nature of the remedy for they described in detail their method of continuous control of gastric acidity by means of "continuous aluminium hydroxide drip". A small Ryle's tube was passed into the stomach and attached to a reservoir of colloidal Aluminium Hydroxide which was allowed to drip into the stomach at 5 to 6 drops a minute, day and night, for a period up to a week or more. They claimed many advantages and excellent results for this "additional refinement of technique in medical management" and considered it indicated in intractable cases prior to operation, and cases with much pain at night. "If", they said, "reliance is placed in antacid therapy, there is every reason to carry it out in the most thorough and continuous manner". This, again, is quoted as an interesting example of transatlantic therapeutic enthusiasm.

Ivy and his co-workers (1937) however, were not so certain of the alleged efficacy of aluminium hydroxide, and thought that the excellent results obtained by Adams et <sup>alia</sup> Al (1937) might, in part, be due to the natural remission of symptoms, or to the production/



production of a mild gastritis by the drug. They therefore tried to determine its effect on (i) normal dogs and (ii) human beings.

(i) Large daily doses were given to dogs for four months (relatively much greater than those used in peptic ulcer therapy), and it was found that a decrease in the gastric secretory response to a test meal did not occur; on the contrary, it seemed that, under prolonged antacid administration, the gastric secretory mechanism tended to compensate for the buffering action of the drug, because at the end of the period, a slightly higher acid response was obtained to the non-medicated test meal! The health of the animals was unimpaired after 3 to 8 months administration, and the liver contained no excess of aluminium.

(ii) They gave the aluminium hydroxide to healthy students accustomed to stomach tubes:-

6 cases were given alcohol test meal (50 c.c. 7%) control, and then 1.4 gram of aluminium hydroxide. Control of "free" acidity obtained for 45 minutes or longer, but individual variation was marked, and in 4 out of 6 cases there was a tendency to increased acidity following evacuation of the stomach.

6 cases received the usual 3 meals a day, hourly specimens of gastric contents being taken throughout the day. On second and third days Aluminium preparations were given half an hour after the meal and at 10 a.m., 3 p.m., and 8 p.m. "Free" acid was shown to be reduced, but tended to rise one hour before the next meal.

10 cases underwent similar experiments, except that drugs were given hourly and in slightly larger doses. "Free" acid control was correspondingly better, but some cases now showed constipation. Therefore, as was to be expected, aluminium hydroxide had a simple "buffering" action on the hydrochloric acid, and this was more effective according to the size of dose and frequency of administration of the drug.

Friedenwald and Morrison (1937), while commending this drug as probably a safe and effective antacid, state that the results so far obtained require further confirmation.

The experimental work carried out in vitro has already been discussed; here the remedy was found to be less effective than it apparently is when administered therapeutically.

The Silicates as Antacids.

Mutch (1936) noting that Dioscorides (A.D.170) mentioned silicates as therapeutic agents, traces the uses of this group of drugs very far back. It is only in the past 15 years, however, that they have come to be regarded as "ideal" antacids.

According to Adams et alia (1934) it was in France that the substance aluminium silicate was first suggested for this purpose in 1922.

The first reference to experimental work, which I have discovered is that of Paulsen et alia (1927). They presented results of two cases with hyperacidity test meal "curves", to whom had subsequently been given aluminium silicate ("Neutralon") at the beginning of the test-meal, and the effect of this on the subsequent "curve" was compared with that resulting from the administration of sodium bicarbonate and magnesium oxide. They found that aluminium silicate produced the most prolonged antacid effect, with practically no fall below the neutral point and no "secondary" rise in acidity during the latter part of the 100 minute test, such as occurred with both the other drugs - especially sodium bicarbonate.

Next came Filinski (1929) who, as mentioned above, carried/

carried out similar tests on numerous patients (number not specified) and obtained the poorest results with aluminium silicate, and the best results with  $\frac{1}{8}\%$  Hydrogen Peroxide!

E. Becker (1933) discussed antacid agents in general and noted that their influence on the subjective phenomena lasted longer than their neutralisation of "free" Hydrochloric Acid would lead one to expect. This he believed was due to their action on peristalsis and spasm. In particular he noted that as a result of one year's observation calcium silicate ("Gastrosil") was an excellent antacid if given in large doses of 1 teaspoonful to 1 dessertspoonful. Nevertheless the effect of a teaspoonful of this antacid on two fractional test meal curves were shown, and reveal "free" acid control lasting for only 30 minutes and one hour respectively. Pffafenberg (1933) advised continued use of antacid remedies, despite their known transient action, and especially <sup>of</sup> the so called adsorbents, of which calcium silicate (Gastrosil) and (Bismoterran) synthetic bismuth silicate, were probably the best. He stated that they had no deleterious effects on the gastric ferments. No experimental evidence was produced in this paper. Mahler (1934) described once more the adsorption and to less extent the neutralising effect of calcium silicate (Gastrosil), and how it was 7 times weaker than/

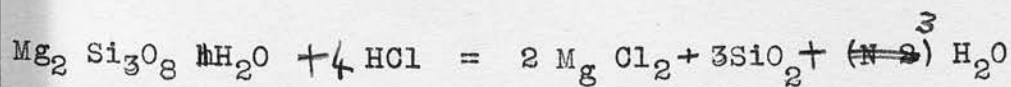
than magnesium oxide in vitro; but, he stated that under the conditions prevailing in the human stomach, the effect of this preparation was much more satisfactory than would have been expected. (Effects on acid responses of two cases were shown to be fairly good - but little ~~of~~ experimental evidence was published regarding this drug as compared with the others tested by this worker (see pages 34, 42.)

K.P. Becker estimated the antacid effects of sodium bicarbonate aluminium silicate, and magnesium peroxide on 3 groups of 10 patients (i.e. 10 patients received one drug, another 10 received another, and so on). He concluded that aluminium silicate diminished the secretion and acidity in all cases, usually by 20% - 25%, and this resulted in an acidity approximating to the normal. In contradistinction sodium bicarbonate and magnesium peroxide, in the average of cases produced no decrease in either. There was also a lasting effect with aluminium silicate, because secretion was still diminished after twenty four hours. He found the mechanism of this prolonged effect very difficult to explain. Frisch (1936) recommended a prescription which contained calcium metasilicate as the chief antacid, and stated that it was cheap and easily regulated for the need of the individual patient. No experimental <sup>was</sup> evidence adduced to support this short paper.

In/



In Britain, Mutch (1936) first drew attention to the silicates as suitable antacids. He investigated numerous silicates regarding their neutralising and adsorbent qualities, and came to the conclusion that the trisilicates, and especially magnesium trisilicate, were the most effective antacids. He found that within the clinical ranges of acidity neutralisation proceeds more rapidly at high acidities than at low ones, that the initial phases of the reaction are rapid, but that several hours are required for its completion in vitro. Regarding adsorption, at room temperature the saturation point for methylene blue was 17 times greater for synthetic hydrated trisilicate of magnesium than for colloidal kaolin, and he believed that this would be even greater at body temperature. Its adsorptive activities extended over a wide range of substances, including alkaloids, putrefactive amines, bacterial toxins and food poison, and this he thought suggested definite therapeutic possibilities. Its reaction with gastric juice is as follows:-



As regards the production of toxic symptoms, this remedy was found to be very satisfactory. Enormous doses were given to mice over a period of months/

months, and no toxic effects or deposits of the drug in the tissues were found.

Doses of 1 drachm to 1 ounce were given to 12 volunteers with no untoward effect; also 1, 2 and 3 drachms were given daily for 3 weeks to 3 groups of 4 volunteers with similar satisfactory results. He therefore concluded that:-

- (1) taken by mouth in relatively enormous doses, this substance was innocuous, and did not disturb the action of the bowels.
- (2) in the stomach, it had a prolonged neutralising action, and the hydrated silica so produced continued to adsorb acid and pepsin, but the latter was still available for digestion.
- (3) in the small intestine, the above adsorptive activities continue, (since this substance has such a prolonged action), and it there acts as a detoxicating agent.

He then treated 15 cases with good results clinically, and also published the results of the effects of doses of gr.xxxv of the remedy on the fractional test meal ( $2\frac{1}{2}$  to 3 hour test) acid response of 10 patients. These results did not show a prolonged or complete control of "free" acidity, e.g./

e.g. there was low acidity for about 1 hour only following the drug. Mutch stated that with the above dose (gr.xxxv) the acidity was kept :-

- (1) at a subnormal level during the entire 3 hour period, when the maximum acidity of the control had not risen above 0.28%.
- (2) below normal for  $1\frac{1}{2}$  hours with maximum control acidities up to 0.33%.
- (3) down over 3 hour period, but not at a subnormal level, when maximum control acidity rose above 0.33%.

On these results he based the following dosage scheme:-

- (1) 35 grs. 3 hourly for acidities up to 0.3%.
- (2) 35 grs. 2 " " " from 0.3% to 0.35%.
- (3) higher doses for extreme cases.

He also suggested that there was a probability that this substance lodged at the ulcer site, adsorbed toxic and necrotic debris, and provided a protective coating against the corrosive and digestive action of acid and pepsin.

In a final paper in (1937) Mutch referred to further work by Mann (1937)(vi) in which complete neutralisation of acidity had been achieved by given 1 drachm/



gram of magnesium trisilicate hourly. He said that such complete neutralisation was widely recognised as advantageous in peptic ulceration; but is rarely required in other cases", and noted how this could not be achieved by milk alone (Kark and Davis (1936) and Mann (1937)). This drug would appear then to be "the ideal antacid", since it is innocuous, can be taken in large doses, is neutral, cannot be absorbed and produce alkalosis or toxic systemic effects, is an effective antacid, and is in addition antitoxic. He noted, however, that occasionally a mild laxative action was present (probably due to the formation of magnesium chloride), and emphasised that medicinal magnesium trisilicate should be the pure synthetic hydrated silicate giving the pure diffraction radio-graph of the natural mineral sepiolite. Many marketed brands fail entirely to conform to these basal requirements.

Further experiments in vitro and one clinical experiment with magnesium trisilicate are reported by Mann (1937). He found that, with excess of dilute hydrochloric acid (about  $\frac{N}{7}$ ), 92% of possible acid neutralisation had occurred in 15 minutes, and little more had occurred in 3 hours. Of this neutralisation 70% to 80% was by direct chemical action, and 20% to 30% was by adsorption.

He/

He found that one drachm = 2 pints  $\frac{N}{20}$  HCl, which is said to be about the average acidity of gastric contents.

If the magnesium trisilicate were in excess, then a pH of 8 was rapidly established and maintained. He finally investigated a case of gastric ulcer (haematemesis) with marked hyperacidity, after 3 weeks intensive alkali therapy. He gave hourly milk feeds (5 oz.) with 1 drachm of magnesium trisilicate mid-way between the feeds. Specimens of gastric contents were withdrawn mid-way between the milk feeds and the trisilicate administration (i.e. at half hourly intervals) between the hours of 7 a.m. and 4.30 p.m. There was no "free" hydrochloric acid present throughout the test. A similar test was performed without the drug 3 days later, when considerable "free" acidity was found to exist. This investigation, however, presents the results of only one case, no comparison with any other antacid (except milk) was made, and the large doses of the drug followed too frequently upon one another to allow any possible secondary acid - stimulant effect to be demonstrated.

The only other references to this group of drugs are those of Friedenwald et alia (1937), who stated that further investigation of their action was required, and Clark (1937) who simply stated (p.298) that/



that magnesium trisilicate had been advocated and was probably effective, but neither provided any further evidence of its efficiency.

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MILK AS AN ANTACID.

Cruveilhier in 1832, first emphasised the importance of milk as an antacid, and since then it has been included in almost every scheme of antacid treatment. Freezer et al (1928) demonstrated its effect in vitro as already mentioned.

In 1936 Kark and Davis confirmed the work of Winkelstein (1933), (1935), when they found that complete achlorhydria could be produced by a continuous drip into the stomach of 5 oz. of milk hourly, and that this result was better than could be achieved by similar amounts hourly by mouth, or by duodenal feeding according to the method of Einhorn. Winkelstein (1933), however, had added sodium bicarbonate to his milk drip so that the patient received 15 grams in 6 quarts of milk daily. Wosika and Emery (1936) found that the milk and cream feeds of the Sippy regime had a good antacid effect when given without the powders, and that the addition of the latter caused only a slight difference in the "free" acidity in their twelve hour tests.

Thus the excellent antacid qualities of milk so long claimed appear to be experimentally confirmed.

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The importance of "free" acidity in peptic ulcer  
genesis as illustrated by recent research.

Recent research concerning the etiology of peptic ulcer has, in almost every case, tended to emphasise the great importance of the acidity of the gastric contents in the production or maintenance of the lesion, and the importance of the failure of the physiological mechanisms by which the body tissues are protected from prolonged exhibition to acid of high concentration. A full discussion of this research does not fall within the scope of this work, but reference may be made to the important experiments of Mann and Williamson (1923) who diverted the alkaline secretions of the duodenum to the ileum, and anastomosed the pylorus to the jejunum. In fourteen out of sixteen dogs operated upon, typical chronic peptic ulcers developed in the jejunum just beyond the pylorus. This has been confirmed in similar experiments by numerous other workers. Mann and Bollman (1932) add that those ulcers will heal if protected from the acid gastric contents by closing the pylorus and gastroenterostomy. Florez and Harding (1933) emphasised the importance of the highly alkaline duodenal secretion which is normally stimulated by the entrance of hydrochloric acid into the/

the duodenum. Failure of this secretion, they thought might be a factor in ulcer production, the acid being thus allowed to act on an unprotected and susceptible mucosa.

Matthews and Dragstedt (1932) and Dragstedt (1936) emphasise the importance of the level of the "free" acidity" in determining the digestion of living tissues by a mixture of pepsin and hydrochloric acid, the concentration of the former being relatively unimportant. Forty two clinical units of "free" hydrochloric acid would appear to be the critical level above which living tissues, even the stomach mucosa, are digested by the above mixture, and it is significant that this is by most authorities recognised as the upper limit of normal "free" acidity. Dragstedt stated that all living tissues (including the stomach mucosa itself) succumbed to the pure undiluted secretion of the fundus, and suggested that in individuals with hyperacidity and hypersecretion the mucosa was exposed for considerable periods between meals and during the night to the action of this pure undiluted secretion - this leading to peptic ulcer. (One would expect ulcer to be more liable to occur if the mucosa were temporarily damaged, for example by a "gastritis"). Dragstedt et alia actually found that when a separate stomach sac was formed/

formed containing only its own pure secretion and an ulcer formed in this sac. Furthermore, in a review of this work, Hadfield and Garrod (1938) pointed out that "the distribution of peptic ulcer corresponds to those areas which are bathed for long periods in acid chyme", and that "whether chronic ulcer ever develops in an achlorhydric stomach is exceedingly doubtful, while peptic ulcer is unknown in association with pernicious anaemia, a disease in which achlorhydria is constant". Of course the ultimate cause of the original disorder of secretion or whatever this may be is quite unknown; Rushing (1932) has suggested a hypothalamic lesion as the primary cause, and the "neurogenic" theory of peptic ulcer genesis has recently received much attention.

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### The rôle of antacids in therapy at the present time.

Almost every page so far discussed has indicated the desirability of employing some antacid drug in the treatment of peptic ulcer and hyperacidity, while the preceding section would seem further to emphasise the importance of adequate "free" acid control to aid healing of such ulceration. Although the necessity of giving drugs is by no means universally admitted, current text-books of medicine and therapeutics and the literature generally almost without exception, advocate their administration.

With regard to the standard text-books, the works of Cushny (1936) and Clark (1937) have already been mentioned, numerous antacids being suggested for a peptic ulcer régime, Hurst, Price (1937) gave sodium citrate with two hourly milk foods, magnesium trisilicate between the feeds and at night (half a drachm), magnesia (five grains in emulsion) often enough to regulate the bowels, and atropin sulphate  $\frac{1}{150}$  grain three times in the twenty four hours. (Olive oil and cream are also included).

Beaumont and Dodds (1936) advocate a modified lippy Régime with two hourly milk (citrated) feeds and a powder of magnesium hydroxide, prepared chalk and bismuth carbonate in equal parts between the feeds./

feeds. In Osler's "Principles and Practice of Medicine" McCrae (1936) advises a Sippy Régime at first, mentioning the use of the neutral phosphates as good antacids (p.479). He gives a choice of methods, however, and also advocates, in certain cases, such remedies as histidine, mucin, and artificial Karlsbad salts. For hyperacidity, larger doses of magnesia and the other usual antacids are advised (p.498). Cheney (1937) gives the usual dietetic régime (p.57) with powders consisting of magnesia, sodium bicarbonate and bismuth subcarbonate. In severe cases the full Sippy Régime is advised (p.60), while in hyperacidity cases similar diet and powders are prescribed (p.165).

On the other hand numerous experienced clinicians have now ceased giving powders with their dietetic régimes, because of their transient antacid effect and undesirable after effects, but few have published their views. Witts, (1937) for example, stated that he gave powders only if the patient complained of pain, in peptic ulcer cases complicated by haematemesis.

In conclusion, the work of Palmer (1930) is noteworthy. He tried to estimate the value of acid neutralisation in peptic ulcer treatment, and mentioned the conditions which make assessment of any line of treatment difficult, e.g. the spontaneous remissions, the fact that rest in bed always helps,

e/

the difficulty of telling objectively when the ulcer has healed, and the impossibility of telling subjectively. From preliminary work he concluded that the effective irritant, and the one responsible for ulcer distress was "free" hydrochloric acid in adequate concentrations acting over an adequate period of time". He then treated two groups of ulcer patients, trying to neutralise the acidity completely in one group, and stimulate ~~it~~ with beef-tea feeds the acidity of the other. The spontaneous pain disappeared in 2.6 days (average) in the first group and 26.6 days in the second. He believed that the desensitisation of the pain producing mechanism indicated some progress in the healing of the ulcer, and so concluded that the alkali group were presumably healing more quickly.

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## SUMMARY OF CHAPTER II.

### THE ANTACIDS.

A review of the literature.

The experimental work on the effects of the antacids prior to the introduction of the fractional test meal is first discussed. The conflict of opinion towards the end of the nineteenth century is noted. Pawlow's important work on dogs was done about this time in which he demonstrated the satisfactory effect of sodium bicarbonate as an antacid.

The actions of antacids in vitro is next considered and the writer's results tabulated. Most workers seem to be agreed as to the relative efficiency of the various remedies. Of neutral antacids, magnesium trisilicate was found to be good but less potent than the work of Mutch led one to expect. Tribasic magnesium phosphate was found by most investigators to be most potent, while aluminium hydroxide had a very poor effect in vitro. Amongst the "older" antacids magnesium oxide was found to be by far the most powerful and sodium bicarbonate, though much less effective, was much more powerful than the neutral antacids. Thus the Sippy Powders are more powerful in vitro than the newer remedies.

The experimental work since the introduction of the fractional test meal is next discussed. Crohn's work demonstrated the unsatisfactory effects of the "alkalis" with their excessive neutralising action followed by acid secretion stimulation. These results



results were confirmed by other workers and this led to the institution of a search for the "ideal" antacid. Tribasic magnesium phosphate and allied drugs were advocated on theoretical grounds and were found to be satisfactory clinically by a few workers, but no very precise evidence of their efficacy was adduced and they were not generally adopted. Much work continued to be done on the older remedies, but little was added the findings mentioned above: this work is reviewed critically. Meanwhile many "ideal" antacids had been introduced and investigated mainly in America and on Continent, and these along with milk are reviewed separately.

The recent experimental work illustrating the excellent properties of milk as an antacid is noted.

Tribasic magnesium phosphate and related drugs are discussed. They were generally found to be very satisfactory but this opinion was based mainly on clinical impressions. It was therefore decided to include this drug in this investigation.

Aluminium hydroxide has been much investigated in America and on the Continent but little or no mention of it is made in British Literature. Its reported excellent effect in vivo belies the results universally found in vitro, but nevertheless almost all the evidence suggests that it is a good antacid. Ivy's careful investigation leads one to believe that it acts simply by virtue of its direct local neutralisation of acidity, and seems to disprove many of the more extravagant



extravagant suggestions which have been made regarding its effects. It was decided to include it in this investigation.

The silicates are next discussed. Aluminium silicate and calcium silicate have been frequently investigated on the Continent in the past ten years, usually with most satisfactory results, but it was in 1936 that Mutch introduced magnesium trisilicate to the profession, and demonstrated its excellent antacid potentialities in vitro. He included a few clinical experiments in his work, but these results were not so convincing. Mann (1937) investigated one case and showed its efficacy as an antacid in large doses. Hence therefore the actions claimed for this remedy in vitro have not yet been investigated clinically it has been made the subject of special study in this work.

Finally a section is devoted to a review of some of the many recent researches which emphasise the importance of high "free" acidity in the stomach in the pathogenesis of peptic ulcer, and the present conflicting views of authorities on antacid therapy set forth in the literature and standard text books are discussed. A consideration of the evidence so far available leads one to the conclusion that, in the early stages of peptic ulcer therapy at least, the antacids have a definite part to play.

CHAPTER III.THIS INVESTIGATION.

Description: discussion: fallacies: description of  
the case histories and charts.

Firstly an outline of the nature and aims of the  
Investigation will be given, and then the details and  
rationale of the work will be explained and discussed.

An endeavour has been made to demonstrate the  
effects:-

- (a) of a single dose of various antacids (usually three) on the acid response to a three hour gruel test meal in the same patient;
- (b) of hourly doses of the same antacids on the "free" acidity remaining after hourly milk feeds had been given as in the Sippy régime. This latter test followed directly upon (a) and extended over a period of nine hours, the whole test therefore lasting twelve hours.

Each patient was, if possible, investigated on four days if the "control" test indicated that sufficient "free" acid remained un-neutralised by the milk feeds. On the three test days following the "control" a different antacid was administered.

Twenty four cases have been investigated; six received only the "control", while eighteen submitted to all four tests. The following antacids have been included:- magnesium trisilicate, Sippy powders No.1 and No.2, (modified), tribasic magnesium phosphate, aluminium hydroxide, and milk.

Preparation of the patient before and control  
between the tests.

On each night and morning preceding a test the patient was prepared for an ordinary fractional test al with restriction of fluids and so on, as scribed by Bennett and Ryle (1921). In addition, the day prior to each test, and on the days usually one) elapsing between each test, the patients re given the following diet:-

Diet for day before and days between tests.

- a.m. Milk 3 oz.: Cream 3 oz.;  
 Strained porridge (1 teacup) Crisp Toast (one slice) buttered, cold; weak tea - 1 cup.
- a.m. Milk 3 oz.: Cream - 3 oz. with switched egg.
- p.m. Milk 3 oz.: Cream 3 oz.  
 Strained fish 3 oz. with white sauce.  
 Milk pudding - 3 oz.: orange juice 1 oz.  
 Crisp toast -  $\frac{1}{2}$  slice.
- p.m. Milk, 3 oz.: Cream 3 oz.  
 1 egg lightly boiled or poached.  
 Crisp toast - 1 slice buttered, cold:  
 1 cup weak tea.
- p.m. Milk 3 oz.: Cream.: 3 oz.  
 Milk Pudding - with one egg, or custard or switched egg.

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No drugs were administered during the period of



the tests except, if necessary, liquid paraffin.

The great majority of the specimens were actually withdrawn and the whole test closely supervised by the writer, who tested all the specimens. The acidity was tested against  $\text{N}/10$  NaOH in the usual way. In some of the tests the antacid produced an alkaline reaction in the stomach contents: the extent of this was estimated against  $\text{N}/10$  HCl.

The patients were encouraged to rest quietly, read and so on, and generally to disturb themselves as little as possible on account of the tests, which appeared to upset them to a surprisingly small extent.

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Details and rationale of the investigation.

criticism of previous investigations of this nature.

In the preceding chapter the papers of previous workers have been individually criticised, and only certain points of importance which have been considered in planning this investigation will be recalled now.

It has been noted frequently that too few cases are reported in many of the investigations (often four or eight, sometimes only one or two), for the conclusions drawn from them to have more than a suggestive value. In numerous cases no definite number of cases was mentioned, in others only theoretical considerations, vague clinical impressions, some experiments in vitro have led to the commendation of a new antacid remedy. While it is desirable that sound theory should precede clinical trial and experiment, too often the latter has been most omitted or inadequately performed. Few workers have compared the new remedies such as aluminium hydroxide with the older ones, such as calcium carbonate, in an adequate series of cases.

In estimating the effect of a given remedy, the test employed has frequently been of too short duration, e.g. one and a half hours, for possible secondary/



secondary after effects to be observed.

It seems desirable, too, that before coming to a conclusion regarding the special effectiveness of any remedy it should be investigated under conditions such as will obtain when it is administered in practice, and that its effect then be compared with other remedies under the same conditions. As the following description relates, an attempt has been made to avoid as many of these sources of fallacy as possible.

The details of the investigation - description;  
rationale, technique, and possible fallacies.

As already mentioned, the first investigation consisted of "the control" test. Patients selected were usually such as one expected to have a high "free" acidity, although several "normal" cases have also been investigated for comparison.

In the initial portion of "the control" a gruel test meal was given according to the method of Alfuss (1914) as modified by Bennett and Ryle (1921), the attention being paid to the preparation of the patient and the precautions during withdrawal of specimens emphasised by them. The patient was permitted to swallow saliva throughout the test  
ence/

nce it has been shown (Bell et alia, 1923) that the neutralising and diluting effect of saliva on the gastric acidity is slight, and furthermore one desired to maintain conditions as nearly as possible those present normally after a meal; also, the duration of the test (twelve hours) rendered the alternative impracticable. Either after the gruel or after one of the first four specimens (usually the second) two ounces of water were given, since the acids were added to this amount on subsequent days. It was taken to try to remove approximately the same amount in each specimen (5 c.c. to 10 c.c.). Twelve hours was chosen as the duration of the initial test so as to allow time for the single dose of the acids studied on subsequent days to manifest their immediate and secondary effects. The tip of the tube when once in a satisfactory position was not again moved if this could be avoided since gastric contents moved simultaneously from different parts of the stomach which have frequently been shown to give completely different acidity values. This has been shown by Johnson (1925), Hubbard and Mumford (1925), and Hie (1929); the latter noted that if the tube were in the lower part of the stomach a more constant and accurate estimate of stomach function might be made.

In this investigation, to have X-ray confirmation

of the position of the tip of the tube has not been possible, but the tube was allowed to pass for some distance beyond the fundus, and was kept at the same position on each day throughout the tests.

Even with the tube externally and internally at the same position it has been shown that different samples of gastric contents withdrawn in rapid succession will have, on occasion but not usually, widely different acid concentrations due to the fact that, especially in the fundus, the stomach contents are not a homogeneous mass. This has been demonstrated by Gorham (1921), Wheelon (1921), White (1922), who suggested that this gastric contents analysis formed only a rough method of estimating gastric secretory function. Similar work was carried out by Kopeloff (1922) and Friedenwald (1924) who were, however, more optimistic regarding the value of the test. The former considered that there was a similarity in all specimens removed in rapid succession and that, if the tube's position were constant a characteristic curve would be obtained. Friedenwald agreed with this provided the tip of the tube be in the pyloric antrum, or, at least, beyond the fundus. It is obviously important to establish this point in the "control" tests used in this investigation so as to be considered of any value.

At/

At this point then, it is convenient to consider the validity of the control test, i.e. the question of its probable constancy from day to day.

Early workers found that if patients were accustomed to the tube, and had great difficulty in swallowing it, a different secretory response (due presumably to central nervous influence) was obtained than that on subsequent occasions when they had become accustomed to it, (Bennet and Ryle (1921)). In this series, therefore, the patient as a result of practice, had no difficulty in swallowing the tube before his "control" response was considered acceptable. In nearly all cases, the first part of the control tests was carried out twice, whilst the stimulating juice and initial two specimens withdrawn each subsequent test day before the antacid was given, served to indicate whether the original control result had been characteristic.

The validity of a single gastric analysis has been frequently questioned. Bennett and Ryle (1921) found that the test meal curve for the same individual was remarkably constant, but Lyon et alia (1921) did not agree with this view. Bell and McAdam (1923) tested one individual on twenty successive days and obtained a very constant result, while Bloomfield and Keefer (1924), using histamine as the acid stimulus and for the tests, concluded that a person's gastric

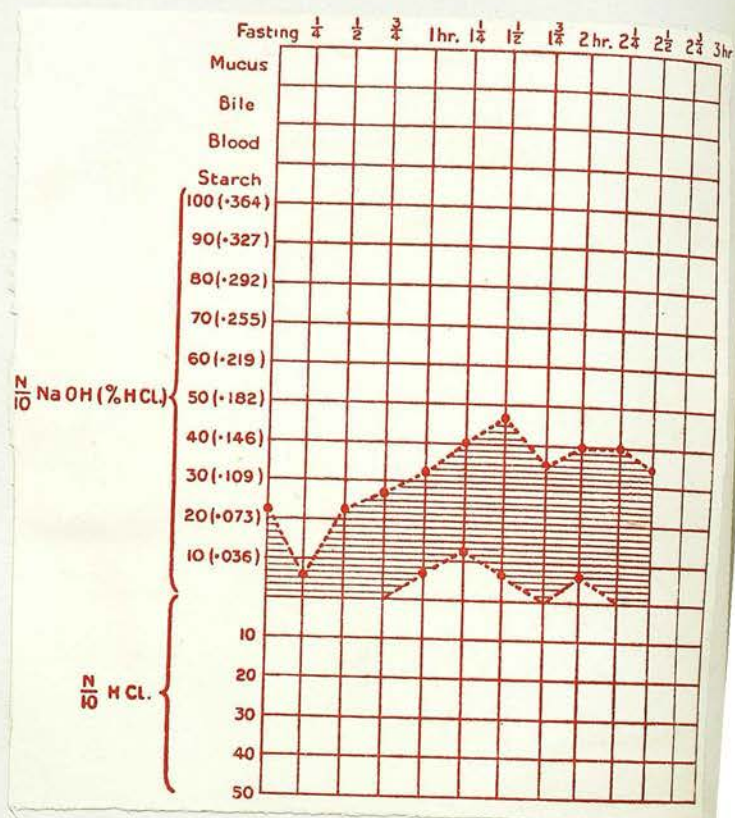


stric acidity response was as characteristic as his finger prints! This latter would certainly not apply to the acidity response to the usual gruel test al.

Vanzant et alia (1931) studied test meal results from two "normal" women over a period of several months and found that a single test might be misleading. There was not usually, however, a marked variation from day to day. The case which showed considerable fluctuation at one period of the test had at the time passed through a period of considerable emotional stress. Hellebrandt et alia (1935) investigated three cases on 8 to 21 occasions with gruel, histamine, and alcohol used as stimulants. They concluded that the secretory response of the stomach is highly variable in the normal subject.... and that since acid secretion is effected via motor, mechanical, chemical, vascular, humoral and reflex paths beyond satisfactory control, and by changes in the physical fitness and general condition of the patient, the estimation of functional capacity in terms of acidity response to a test meal..... is not a valid procedure."

At the same time one noted that, although the acidity responses varied somewhat over the considerable period during which their patients were tested, this variation did not at any time exceed 10 clinical units either side of the average for each individual.





THE SHADED AREA REPRESENTS THE LIMITS FOR  
"FREE" HYDROCHLORIC ACID IN THE FRACTION  
TEST MEAL (GRUEL) RESULT IN 80% OF NORMAL  
PEOPLE.

(BENNETT AND RYLE, 1921.)

One imagines that in the present investigation, which was, in almost every case, completed within a week under very constant conditions, the variability would have been shown to be less.

The initial part of each test which, it will be found, acts as a control on each day confirms this in almost every case. Furthermore, nearly all the patients had a double initial test meal, and results were nearly always found to be very similar. (These "double controls" have not been charted in every case owing to the overburdening of the charts so caused). However, as treatment proceeded, most cases showed a slightly higher acidity. This is in accordance with the findings of Hurst and Venables (1929), but this slight variation would not greatly affect the results or conclusions regarding the antacids' effects.

The question of what could be considered a "normal" fractional test meal response has had to be reviewed before this investigation could be begun, the cases selected, on the results classified. Bennett and Ryle (1921) studied very carefully one hundred healthy males from this point of view, and their chart of the wide limits of "free" acidity is shown on the opposite page; this is probably as good a guide as we yet possess to what may be considered "normal". Various factors have been found to influence the maximum/

ximum level of "free" acidity in people with healthy  
 gastro intestinal tracts, the chief of these being  
 constitution, age and sex. Vanzant et alia (1932)  
 studied a large series of "normal" Ewald Test Meal  
 results (3,767) and concluded that for adult healthy  
 males 45 to 50 clinical units should be the average  
 "free" acidity, 35 units for adult females, and 30 to  
 units for aged males; but the "normal" range for  
 both sexes was 90 units! Sagal et alia (1933) in an  
 even larger series obtained similar results. The  
 investigations of Pierce et alia (1932) and Pollard  
 et alia (1931) using histamine or alcohol tests served  
 to show the wide variation in normal individuals and  
 the impossibility of setting well defined "normal"  
 standards. Davies et alia (1930) again demonstrated  
 a tendency for acidity to decrease with age, and  
 an increase in achlorhydria which occurred in normal  
 males studied in later life. The relations of gastric  
 acidity to height and weight, and even to the seasons  
 were studied by Vanzant et al (1937), (1932), but no  
 significant results were obtained. In view of the  
 previous investigations it was decided in this series to  
 include any case in which the "free" acidity rose above  
 the clinical points a case of hyperacidity. (The  
 indicator used was Thymol Blue, which gives "free"  
 acidity readings 3 to 5 points lower than Topfer's  
 indicator ~~used~~ in the above investigations).



The choice of a test meal.

Many substances besides oatmeal gruel have recently been advocated as more effective stimulants of acid secretion. These include alcohol, histamine, tea with toast or biscuits, meat extracts, and so on. It was decided, however, to use gruel in these investigations, because, although it is unpalatable and perhaps tends to lead to a low acidity response, it is the only one for which even approximate standards of normality exist, and it is the one which has most frequently been used in similar experiments in the past; comparison of results is thus made possible.

The gruel was prepared and the test performed as described by Bennett and Ryle (1921); care was taken to see that exactly one pint was taken. 5 c.c. to 10 c.c. specimens were withdrawn at intervals of 15 minutes, and the test was carried on for three hours. After one of the early specimens, usually the second, two ounces of water were taken as this was the amount in which the drugs were administered on subsequent days. Immediately after the second specimen was found to be most suitable time at which to give the drugs, since it allowed of a comparison of the initial part of the test with the control results/

results, and at the same time, left a two and a half hour period for the study of the action of a single dose of antacid on the acidity response to the test meal.

In the succeeding nine-hour part of the test milk feeds were given hourly with water (nearly always one ounce) midway between the feeds. On subsequent days the antacid was added to this water. In the first two cases, 5 oz. feeds were given as in Mann's investigation (1937) but this was found to be too large a feed with too great an antacid effect and so the 3 oz. feed was chosen as in the Sippy Régime, but with no cream, as this is often omitted in therapy. Two hourly 6 oz. feeds, being more usually given therapeutically at the present time with antacids between the feeds, might have provided equally if not more useful information, but it was desired to show the effect of a really strict régime first. Milk was of course chosen since it is employed in therapy, and one desired to study its potency as an antacid. It has been shown by Carlson (quoted by Best and Taylor, 1937) to be, amongst foodstuffs, a "medium" gastric acidity stimulant; it was also a convenient substance for withdrawal from the stomach for testing purposes.

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The choice of an indicator.

The indicator Thymol Blue was chosen since it gives a better end-point for "free" acidity (at a pH of about 2) than Töpfer. It was mentioned as an alternative to Töpfer's Reagent by Martin (1934) and recommended by Richardson (1934) and Stewart and Dunlop (1937). Martin pointed out, however, that 0.001NHCl has a pH of 3, and therefore some quantity of "free" acid may be missed with Thymol Blue, and that none of the indicators is really satisfactory for very accurate work.

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the value of the estimation of the total chlorides in fractional gastric contents' analyses as an index of acid secretory activity.

In the present investigation it is obviously of importance to gain some idea of the real acid secreting activity of the stomach if an estimation of the antacid power of a given remedy is to be made. It was at first thought that the total chlorides' estimation did to some extent provide this information with more accuracy than the test meal acidity values, but recent research has definitely tended to disprove this. It was therefore considered unnecessary and inadvisable to carry out this estimation, since its inclusion would entail much extra work, overburden the charts, and, most important, would tend to confuse rather than clarify the results.

#### The relevant literature.

Boldyreff (1914) in animals, and Bolton and Podhart (1922) in man, first showed that when gastric acidity reaches a certain level during digestion, the pylorus relaxes and alkaline fluid from the duodenum regurgitates to <sup>the acidity</sup> neutralise to some extent. They concluded that the fall in acidity in

the later specimens of a fractional test meal was due to this regurgitation along with neutralisation of acid by the alkaline secretion of the pyloric mucosa. These observations were supported by the work of Baird et alia (1924), while Miller et alia (1927) stated that "it has long been accepted that the total chloride estimation is the more accurate index of the secretory activity of the stomach".

A little later, however, MacLean et alia (1928, a, b, and c) and MacLean (1929) demonstrated in a series of researches on dogs with separate stomach pouches where no duodenal regurgitation could occur, and also in man, that the presence of a certain concentration of acid in the stomach inhibits the secretion of acid with the result that neutral fluid containing chlorides is secreted which by dilution reduces the acidity of the gastric contents. Also, Gorham et alia (1928) from work on the human subject concluded that the determination of the total chlorides was not a volumetric index to the production of hydrochloric acid by the gastric glands. Webster (1934) however, found that under normal conditions, the gastric glands never secrete sufficient neutral or faintly acid fluid to dilute the gastric contents and reduce their acidity, but that this was accomplished partly by the alkaline mucus of the surface epithelium, and partly by the secretion of mucoid/

coid material by the peptic glands themselves.  
lmer (1934) also emphasised the importance of the  
acid effect of mucus and considered it was  
esent normally in sufficient quantities to account  
r the main variations in titratable acidity of the  
stomic juice. Nevertheless, the great majority of  
rkers agreed with MacLean. Beaumont and Dodds (1936,  
,) reviewing this literature stated that "the  
portance of duodenal regurgitation has been over  
timated", and investigations supporting MacLean's  
rk include those of Rudd (1931), Goldberg (1932),  
ay et alia (1932), and MacLagan (1934).

It would therefore seem that in the present  
ate of our knowledge the estimation of the total  
lorides would not aid one in estimating the real  
ld secreting activity of the stomach.

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### The Choice of Antacids.

Sippy Powders No.1 and No.2 (modified, as used in the Royal Infirmary, Edinburgh.)

Sippy Powder No.1 consists of:

Magnesium Oxide	)	
Sodium Bicarbonate	)	in equal parts.
Sodium Citrate	)	

Sippy Powder No.2 consists of:-

Sodium Bicarbonate	)	3 parts
Calcium Carbonate	)	1 part

These powders were chosen in preference to the separate drugs since it is in this combined form that these remedies are practically always employed, and it was under therapeutic conditions that it was desired to test them. They are still the most frequently prescribed antacids, and hence it is necessary that they should be included in any selection of antacids to be compared. They are also the least expensive.

Tribasic magnesium phosphate was chosen because of its excellent effect in vitro, its frequent recommendation by other writers, and the fact that it has never been adequately tested in the human subject.

Aluminium/

Aluminium hydroxide has been selected since it is the most effective of the "new" antacids according to most American workers. Furthermore, it has not, so far as the writer is aware, been investigated in this country.

Magnesium trisilicate, - the most recently introduced antacid, has been investigated in every case in which a drug was given (i.e. eighteen) since, while it has been fully investigated theoretically and in vitro by Mutch in this country, it has received little attention elsewhere, and clinically only one case has been investigated (Mann, 1937) in the manner set forth in this work. It would seem on the evidence so far obtained to be the best of the antacids.

Milk. The reasons for the study of milk's antacid effects have already been discussed.

Other antacids, new and old, such as atropin, gastric mucin and so on, have been omitted because either they have been fully dealt with already, or have not seemed likely to be of value, or because comparison with the antacids in this investigation would be difficult on account of the problem of equivalent dosage.

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In the first chart "the control" is shown against the findings for magnesium trisilicate; in the second the control with the Sippy Powder result is indicated: in the third chart magnesium trisilicate is compared with a Sippy Powder, and in the fourth aluminium hydroxide or tribasic magnesium phosphate is contrasted with the control.

The other details of the charts, e.g. mucus, are indicated as follows in the appropriate colour (vi):-











First chart - findings on control test day

Second chart - " " Sippy Powder test day

Third chart - " " Magnesium trisilicate test day.

Fourth chart - " " aluminium hydroxide or tribasic magnesium phosphate test day.

Throughout the charts the results for each antacid have been indicated in different colours, as follows:-

1. "Control" (i.e. gruel and milk) (black)		represents	"free" acidity.	
		"	total	"
2. Magnesium trisilicate (green)		"	"free"	"
		"	total	"
3. Sippy Powders No.1 or 2. (red)		"	"free"	"
		"	total	"
4. Aluminium hydroxide (blue)		"	"free"	"
		"	total	"
5. Tribasic magnesium phosphate (purple)		"	"free"	"
		"	total	"



PRICES OF THE SUBSTANCES USED IN THIS  
INVESTIGATION.

In this work "Magsorbent" Brand magnesium trisilicate, (as recommended by Mutch as being a pure preparation and used by him), was chosen; "Hydronal", (aluminium hydroxide, Bayer) was also employed. Although not yet in the British Pharmacopoeia, pure and much less expensive non-proprietary preparations are now available, and there is no reason to suppose that these drugs would be less effective than the ones employed in this investigation.

Sippy Powder No. I. (modified).	...	4oz.	...	I/-.
Sippy Powder No. 2. ( " )	...	"	...	"
Magnesium trisilicate. (Non-proprietary.)	...	"	...	I/9d.
Aluminium hydroxide. (Non-proprietary.)	...	"	...	I/6d.
Tribasic magnesium phosphate.	...	"	...	I/6d.
"Hydronal" (Aluminium hydroxide, Bayer.)	"		..	I3/5d.
"Magsorbent!" (Magnesium trisilicate, Kaylene, Ltd.)	...	"	..	2/4d.

(Mr. G. Perrins, Chief Dispenser, Royal Infirmary, Edinburgh, has kindly supplied most of these prices.)

If proprietary preparations are excluded it would appear to matter little, so far as price is concerned, which of the antacids be employed, if the effect of one be proved superior to another.



### SUMMARY OF CHAPTER III.

#### This investigation.

An outline of the proposed investigation is first given indicating the nature and aims of the work. Each test consists of an analysis of the gastric contents over a period of twelve hours. During this time a gruel test meal (three hours), and hourly milk feeds (nine hours) are given. Cases are investigated on four occasions, and in the subsequent tests various antacids are given. The effect of a single dose of each remedy on the acid response to the test meal is first investigated, and then it is given hourly between milk feeds to observe its effect when given in a strict therapeutic régime. Thus four antacids are investigated in each case (including milk) and their effects are compared.

The details and rationale of the work are next discussed. The preparation for and control of the patient between the tests is described. Previous work of this nature is criticised briefly, and the steps taken in this work to avoid certain of the faults mentioned are indicated, and such fallacies as remain are noted.

Certain problems not fully dealt with in the preceding section follow. The validity of the "control"/

"control" test, the consideration of the "normal" fractional test meal acid response, and the choice of the most suitable test meal are discussed. The value of the estimation of the total chlorides as an index to the acid secretory activity of the stomach is fully discussed, and the reasons given for its omission in this investigation. The choice of the antacids to be investigated is considered, and the chapter ends with a description of the arrangement of the case histories and charts which demonstrate all the results obtained in the investigation and form the next chapter.

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## CHAPTER IV.

THE INVESTIGATION.The case histories and charts.

In this chapter are set forth the results of an investigation into the influence of certain antacids on the acidity of human gastric juice in twenty four cases by means of fractional gastric contents' analyses extending over a period of twelve hours in each test as described in Chapter III.

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In the following six cases only milk was investigated in each case.

The cases represent varying degrees of "free" acidity from "medium" normal to marked hyperacidity. The milk feeds varied from five to three ounces hourly as indicated on the charts.

They illustrate the excellent antacid qualities of milk but its inadequacy in dealing with cases of hyperacidity.

---



## CASE NO. 1.

MRS A.K.

Aged - 38.

Complaint. Praecordial pain and epigastric pain

Duration . Five years.

Examination. Clinically - negative as regards the  
digestive system.

Test meal - normal acidity.

No further investigation of the  
digestive system.

Wassermann reaction - strongly positive.

Diagnosis. Angina pectoris, syphilitic aortitis,  
and aortic incompetence.

ONLY THE CONTROL TEST WAS CARRIED OUT IN THIS  
CASE SINCE THE FIVE OUNZE MILK FEEDS HOURLY WERE  
QUITE ADEQUATE TO CONTROL THE "FREE" ACIDITY  
COMPLETELY.

Case No. *4*.....  
 Name..... *Mrs. A.K.*.....  
 Age..... *38 yrs.*..... Date..... *3<sup>rd</sup> Dec. 1937.*.....  
 Diagnosis..... *Angina Pectoris : Syphilis.*.....

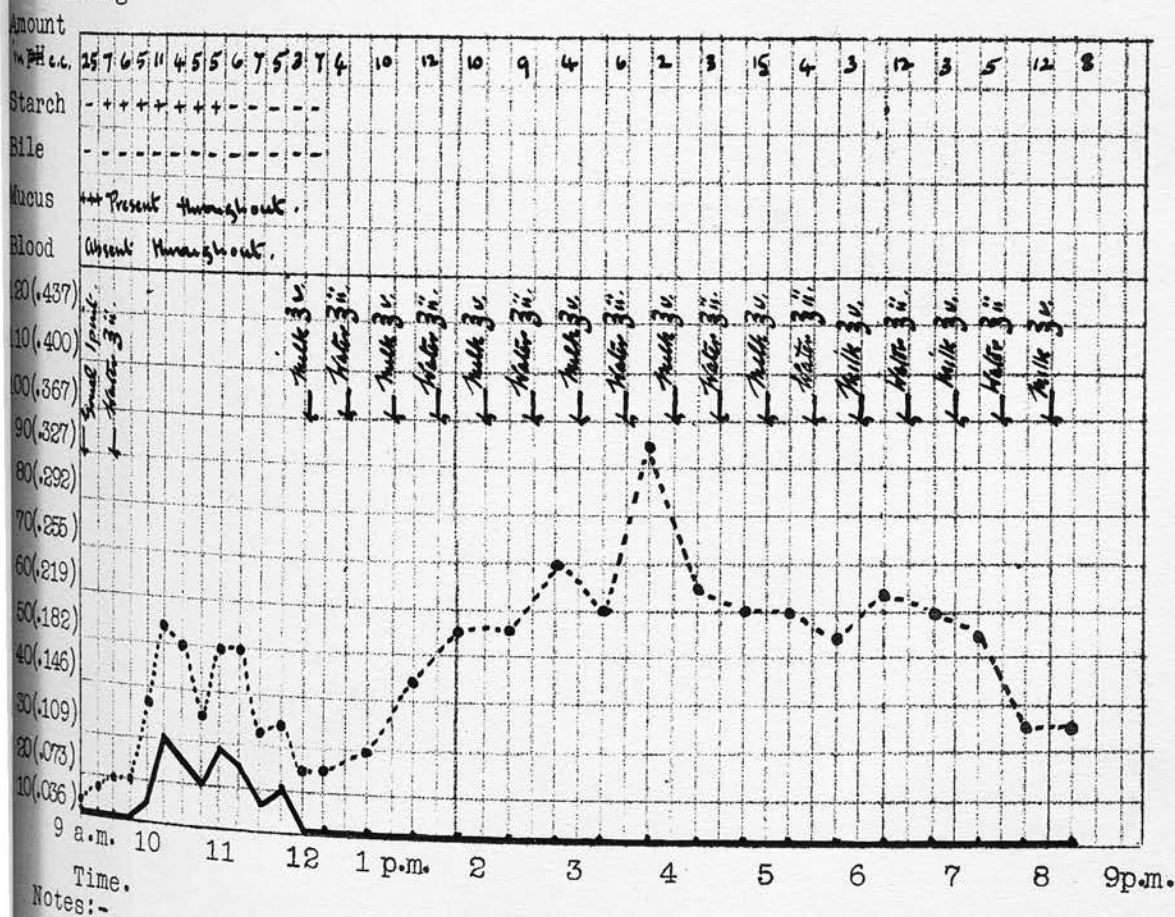
Substances given:-  
 A. "Food". *Food and milk - as indicated.*.....  
 B. Antacid(s). *none - except milk and water - as indicated.*.....

Fasting juice. Amount..... *25*..... c.c.  
 Special Characters... *Mucus. + + +*.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



This chart shows how milk feeds of five ounces hourly will completely neutralise the acidity ("free") in the stomach of a "normal" individual.

MRS J. Mc.C.

Aged - 68.

Complaint. Vomiting blood ... 2 months prior to admission and on several previous occasions.

Examination. Clinically - negative.

Faeces - no occult blood.

Test meal - High normal acidity.

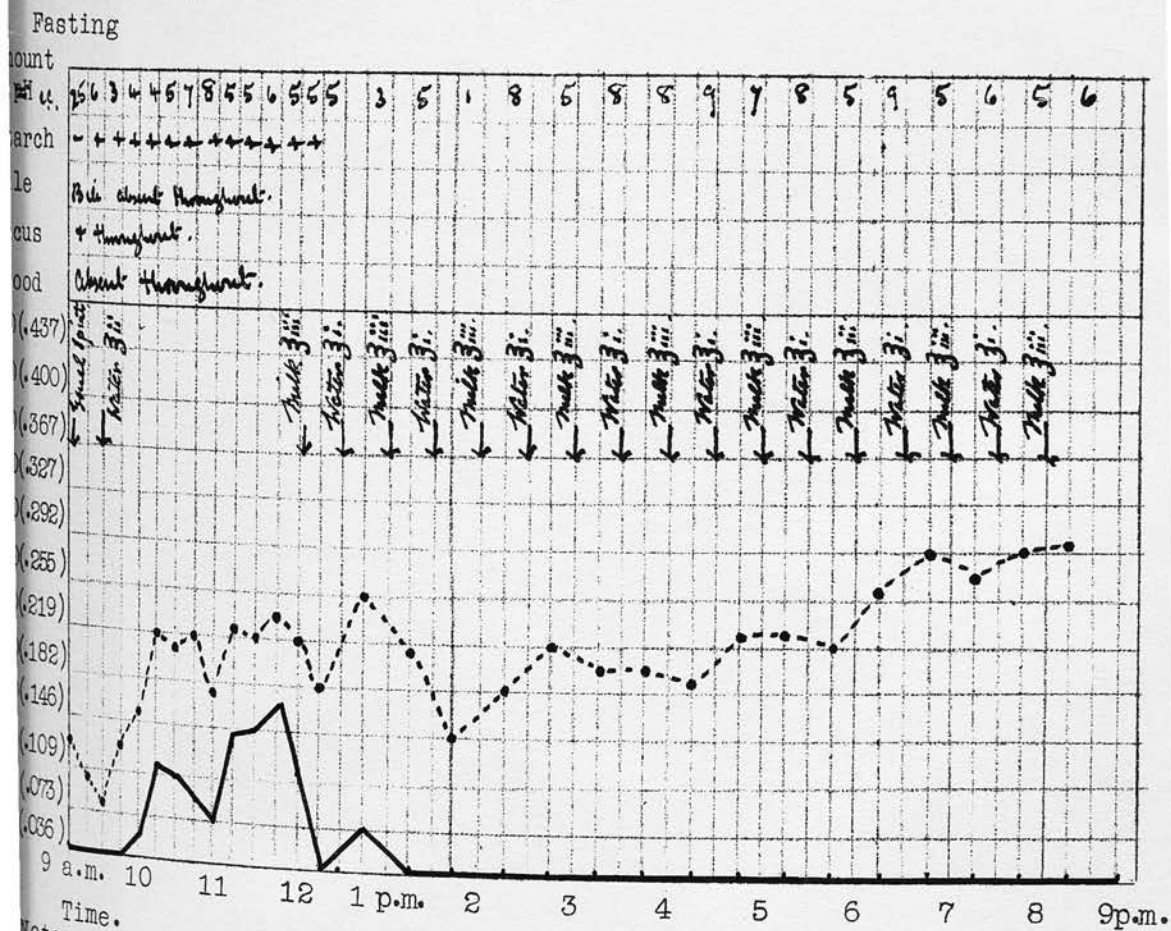
Barium series - persistent incisura on greater curvature probably due to old ulcer scar

Diagnosis. Gastric ulcer.

IN THIS CASE OF HIGH NORMAL ACIDITY CONTROL OF "FREE" ACID WAS ALL BUT COMPLETELY ACHIEVED BY THE THREE OUNZE HOURLY MILK FEEDS ALONE.

Case No. .... 2 .....  
 Name ..... Mrs. J. McB. ....  
 Age ..... 68 ..... Date ..... 28<sup>th</sup> Feb., 1938. ....  
 Diagnosis ..... Gastric ulcer. ....  
 Substances given:-  
 A. "Food". gruel and milk ..... - as indicated. ....  
 B. Antacid(s). none ..... except milk and water. ....  
 Fasting juice. Amount ..... 25 ..... c.c.  
 Special Characters .....  
 Acidity, etc. (See first column below.)

..... represents free HCl.  
 ..... represents total acidity.





CASE NO. 3.

MRS. A.S.

Aged 50.

COMPLAINT. Fullness in the stomach not in any way  
related to food..... 2 years.

EXAMINATION.

Clinically - negative.

Barium series - " .

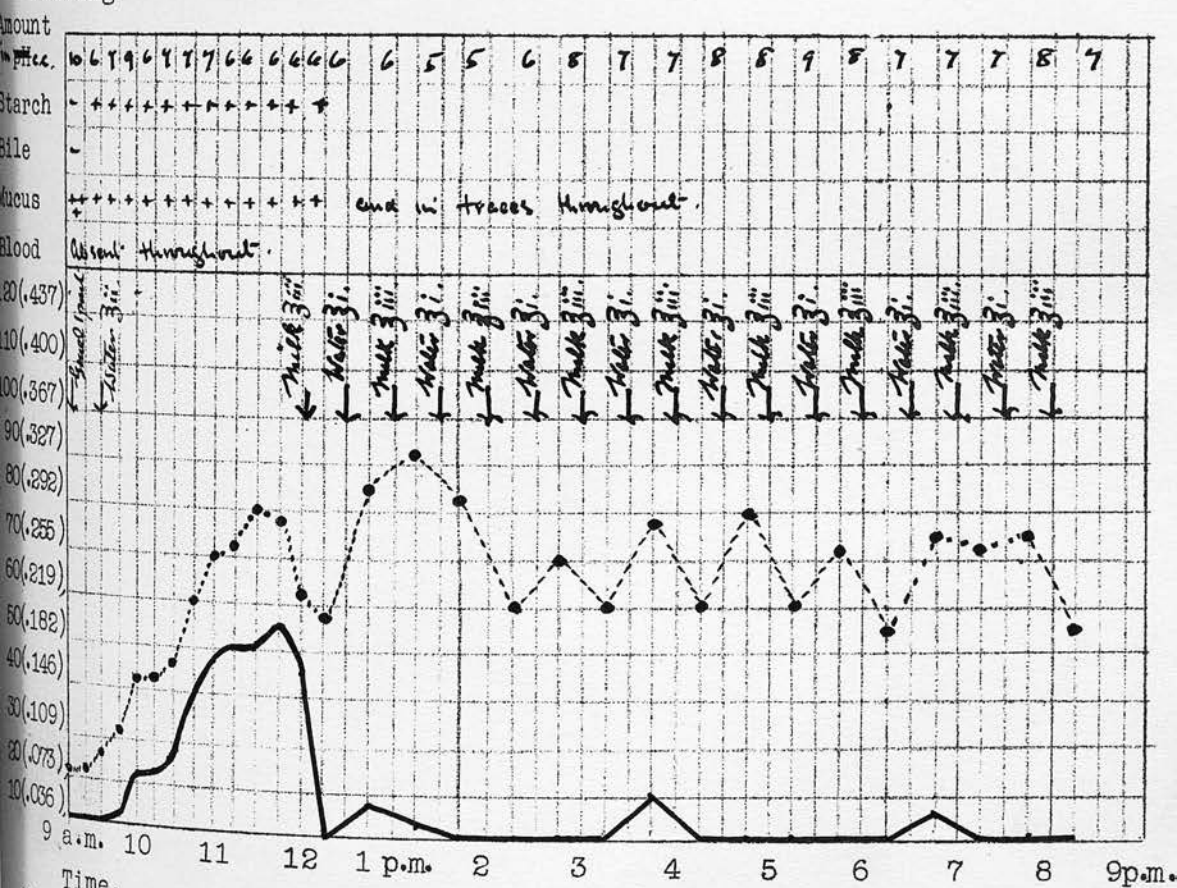
Faeces - no occult blood.

Test meal - high normal acidity.

DIAGNOSIS. Anxiety neurosis.

ONLY THE CONTROL TEST WAS DONE SINCE WITH THIS  
TEST MILK FEEDS OF THREE OUNZES HOURLY THE "FREE"  
ACIDITY WAS ALMOST COMPLETELY CONTROLLED.

## Fasting



Notes:-

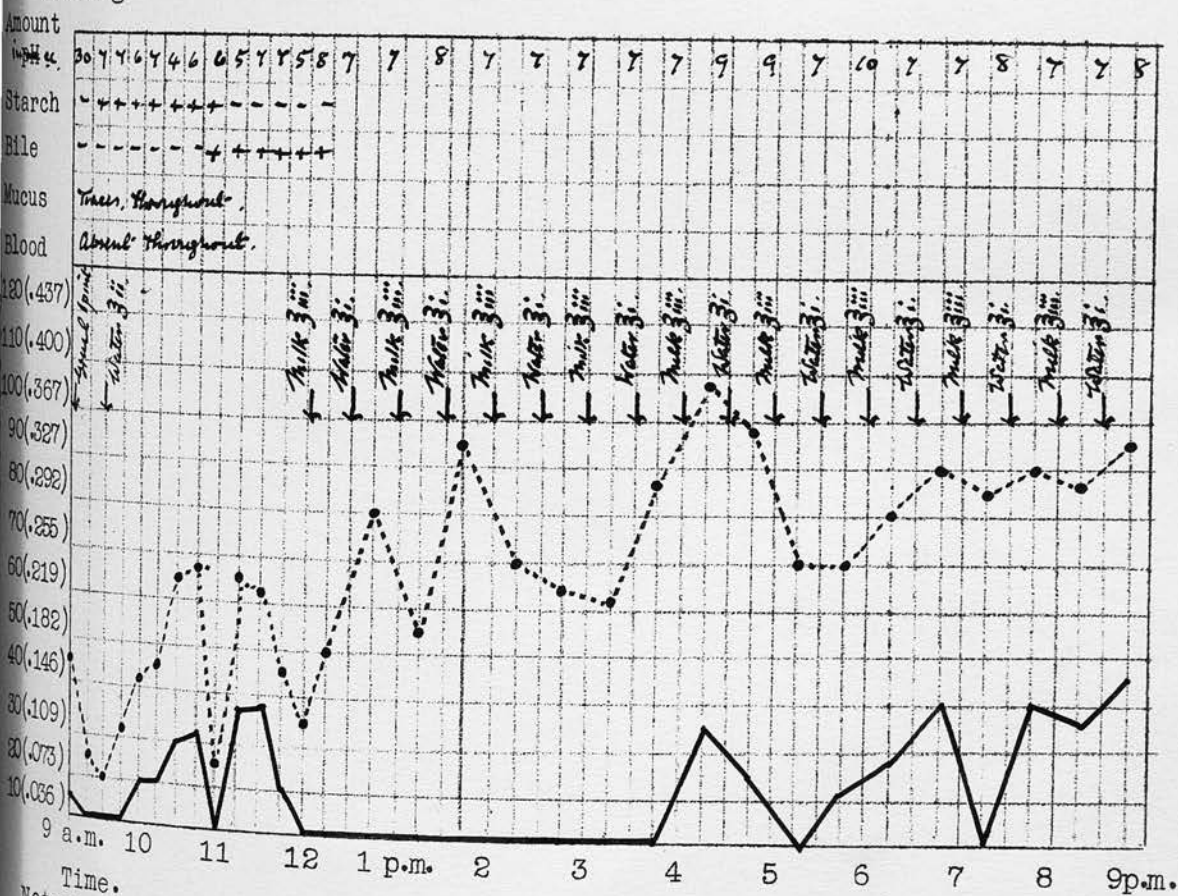
A case of "high normal" acidity which shows the excellent effect of 3oz. milkfeeds without powders in controlling the "free" acidity of the stomach contents.

Case No. 4. Milk feeds only - investigated.  
 Name Mrs. R. F.  
 Age 24. Date 28th. Feb. 1938.  
 Diagnosis Headache - due to refractive error.  
 Substances given:-  
 A. "Food". Gruel and then milk feeds hourly; 3oz.  
 B. Antacid(s). None except milk feeds.  
 Fasting juice. Amount 30. cc. c.c.  
 Special Characters none.  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Shows a case of normal acid response to a gruel test meal with almost complete control of the "free" acidity by three ounce milk feeds hourly.

Although the acidity at the end of the test is not completely neutralised it at no time reaches a level dangerous to living tissue.



## CASE NO 5

MR .F.McK.

Aged - 53.

Complaints. Pain in chest and epigastrium..I week.

Examination. Clinically - Mid epigastric tenderness especially to the right,with rigidity in this area.

Test meal - mild hyperacidity.

Faeces - no occult blood.

Barium series - negative for ulcer atonic stomach.

Wassermann Reaction- strongly positive.

Diagnosis. Hyperacidity and syphilis.

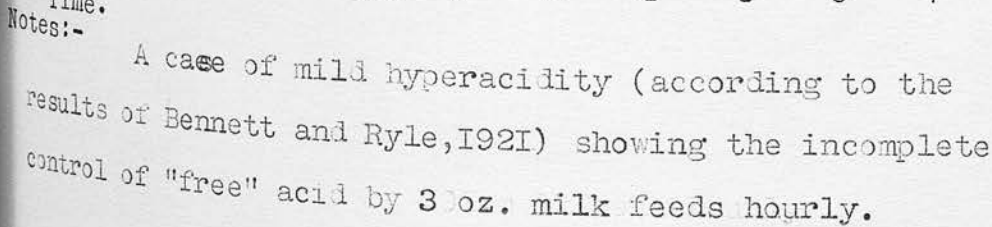
ONE TEST ONLY WAS PERFORMED OWING TO THE PATIENT'S INABILITY TO TOLERATE MORE.

This control test shows a case of mild hyper acidity which was not completely controlled by small hourly milk feeds of three ounces.



Fasting juice. Amount... 56..... c.c.  
Special Characters.....  
Acidity, etc. (See first column below.)

## Fasting



## CASE NO. 6.

MR. T. J.

Aged. - 64.

Complaint. Pain in the stomach ..... 2 days.

"Indigestion" off and on for 5 years

Examination. Clinically - Tender in left hypochondrium and rigid in epigastrium.

Electrocardiogram suggests coronary thrombosis.

Test meal - hyperacidity.

No other investigations available.

Diagnosis. Coronary thrombosis.

ONE DAY GASTRIC CONTENTS' ANALYSIS.

When heart condition was discovered it was decided to discontinue the tests and thus this case was not completely investigated.

The single control test shows a case of marked hyperacidity which was not well controlled by small milk feeds of three ounces alone although considerable antacid action appears to have been exerted.

## ANALYSIS OF GASTRIC CONTENTS.

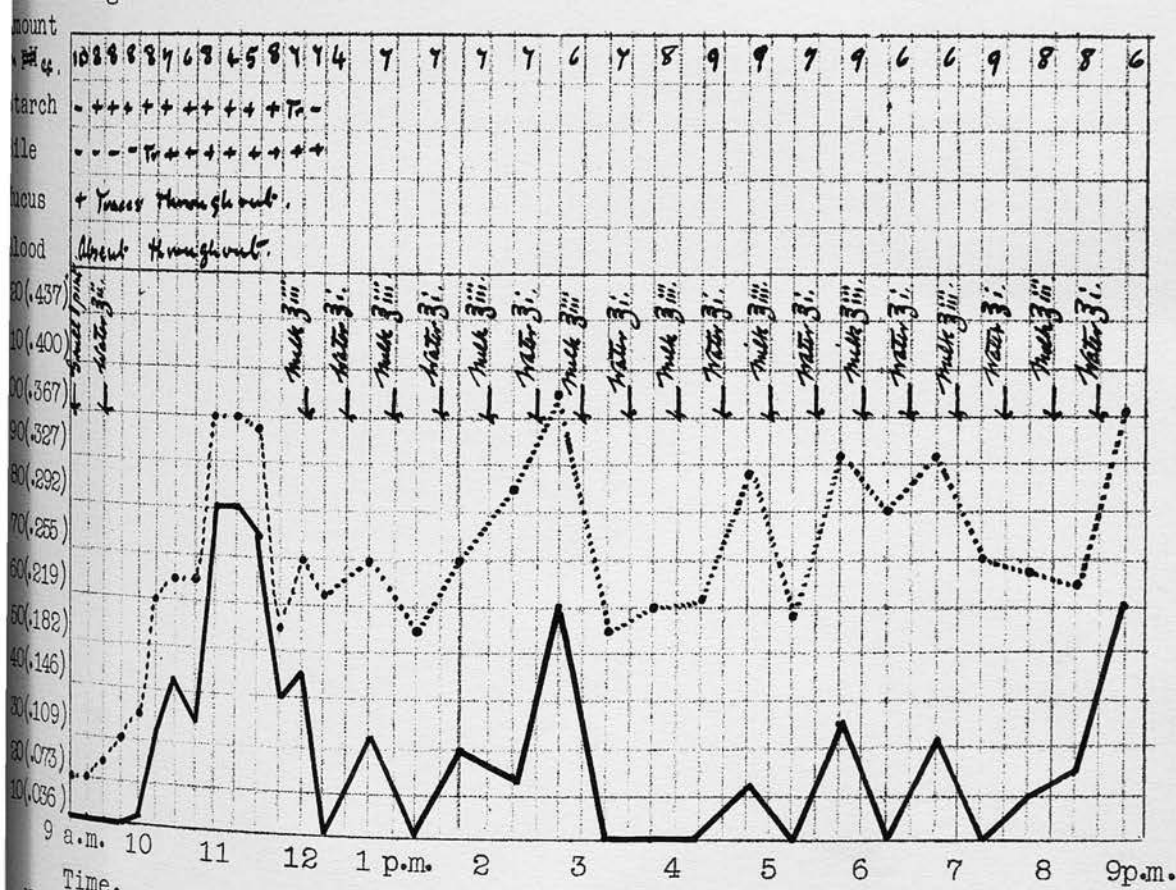
104.

Case No. 6..... Milk feeds alone investigated.  
 Name..... Mr. T. J.....  
 Age..... 64..... Date..... 16th. Feb. 1938.....  
 Diagnosis..... Coronary Thrombosis..... Hyperacidity.....  
 Substances given:-  
 A. "Food". .... Gruel and milk feeds 3 oz.....  
 B. Antacid(s). .... None but milk feeds.....  
 Fasting juice. Amount..... 10..... c.c.  
 Special Characters..... none.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



A case of hyperacidity which shows that small milk feeds while exerting a considerable antacid effect cannot achieve satisfactory control in cases of this type.

Owing to the condition of the patient the case was not studied further.

In the next seven cases milk ("control"), Sippy Powder No.1, magnesium trisilicate, and tribasic magnesium phosphate were given.

In the initial test of a single dose, twenty grains were given at the point indicated.

In the nine-hour test, doses of twenty grains hourly between milk feeds were given.

-----



## CASE NO. 7.

MR. G. S.

Aged - 28.

Complaints - Pains and stiffness in the joints, but  
no dyspeptic symptoms.

Examination - Clinically - nil in digestive system.

No investigations re the digestive  
system except test meal which showed  
moderate hyperacidity in the first  
result.

Diagnosis. Rheumatoid Arthritis.

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

I. Effects of antacids (gr. 20.) on three hour test .  
Control shows normal acidity curve on day of second  
test. Magnesium Trisilicate was effective in con-  
trolling the acid for 45 - 60 minutes with no second-  
ary stimulant action. Sippy No. I. and Tribasic Mag-  
nesium Phosphate were effective for only 15 - 30  
minutes and both, especially the latter were followed  
by a marked secondary acid secretion.

II. Effect of antacids (gr. 20.) hourly on nine  
hour test with hourly 5oz. milk feeds.  
Control showed only a very low acidity on account  
of the excellent antacid properties of the large  
milk feeds but this acid was completely neutralised  
by all three antacids. Sippy No. 2. caused an alkaline  
reaction in the stomach on two occasions, and so  
seemed the least satisfactory powder.



## ANALYSIS OF GASTRIC CONTENTS.

CONTROL - with Magnesium Trisilicate.

107.

Case No. 7.7. ....Name Mr. G.S.Age 28Date 29<sup>th</sup> Nov. 1937.Diagnosis Rheumatoid Arthritis.

Substances given:-

- A. "Food". 1) Breakfast - 1 pint - at 9 am.  
2) Milk - 5 oz. hourly from noon.  
 B. ~~Antacid(s)~~ + water 2 oz. hourly from 12.30 pm. (i.e.)

Fasting juice. Amount 46 c.c.Special Characters —

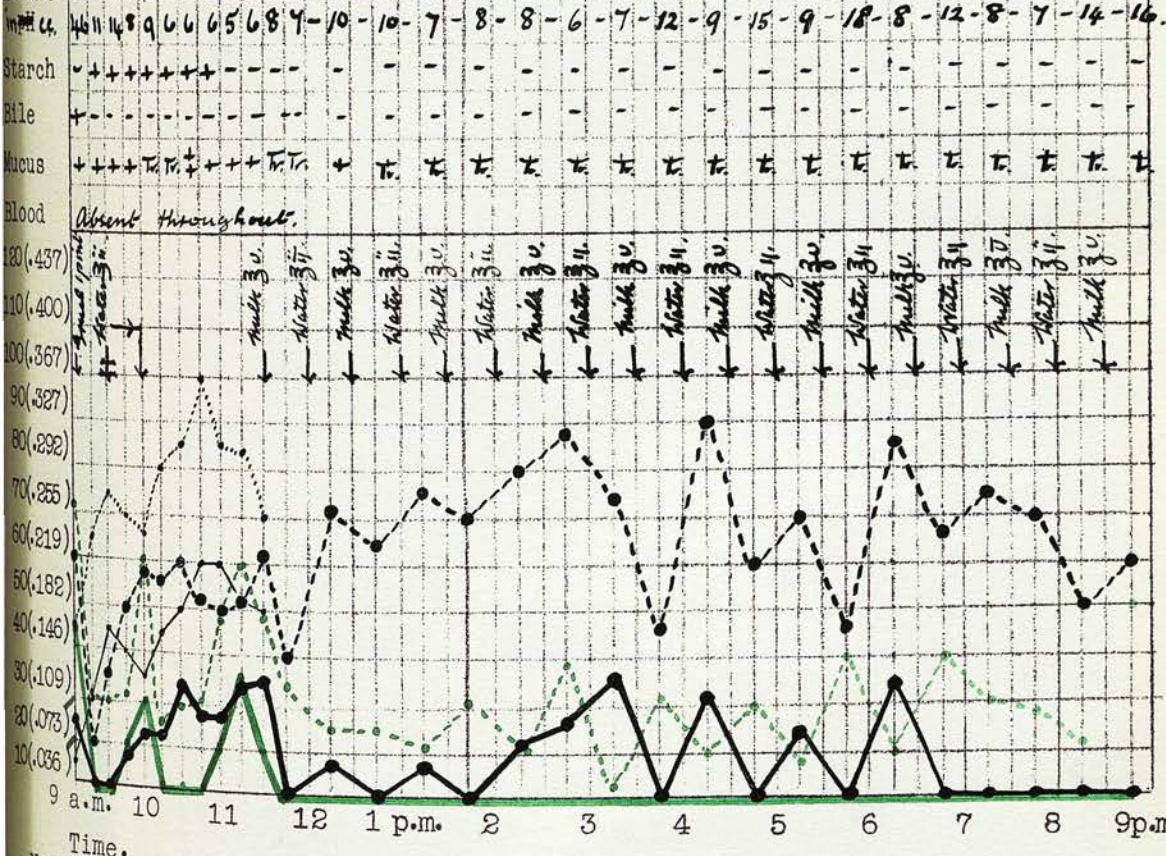
Acidity, etc. (See first column below.)

..... represents free HCl.

.....?..... represents total acidity.

Fasting

Amount



Notes:- Fine double control lines indicate the result of a test meal some weeks prior to the control proper.

Original test meal showed a degree of hyperacidity but the control proper is within normal limits; with 5oz. hourly milk feeds only low "free" acidity was present from time to time. In practical therapeutics a greater degree of acid control would probably be unnecessary.

A dose of 20 gr. Magnesium Trisilicate modified the control result only slightly; during the second part of the test complete acid control was found to have been achieved.



## SIPPY POWDER NO. I. TEST.

Case No. 27.....

Name... Mr. G.S. ....

Age... 28 ..... Date... 1<sup>st</sup> Dec. 1937.....Diagnosis... Rheumatoid Arthritis. .....

Substances given:- ① Equal - 1 pint - at 9 a.m. ....

A. "Food". ② Milk - 5 oz. hourly from noon. ....

B. Antacid(s). Sippy Powder No. 1. - gr. XX in water 3 ii  
as indicated in chart. For comparison v.v. ....

Fasting juice. Amount.... 38..... c.c. ....

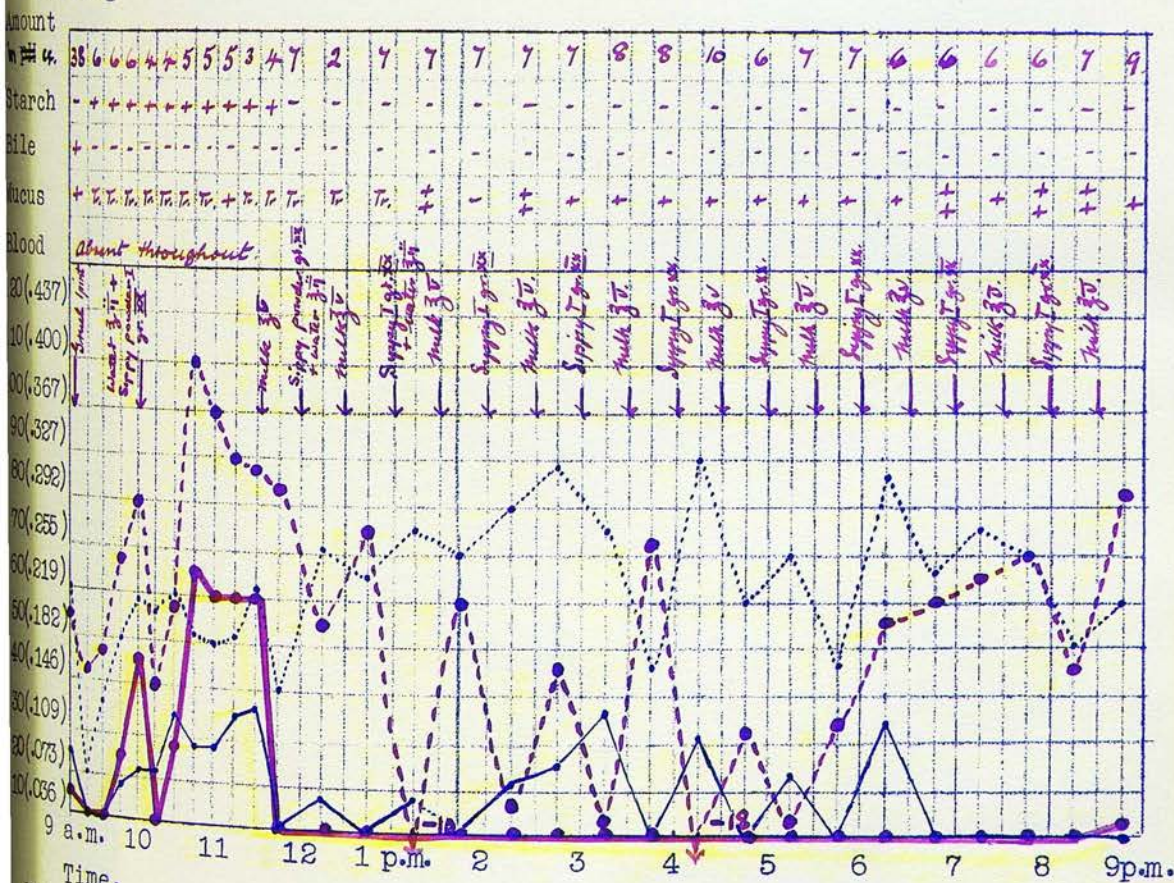
Special Characters..... ..

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- There was no significant acid neutralisation by the 20 gr. dose of Sippy No. 2., but its administration was followed by a considerable secondary acidity secretion.

During the remainder of the test no further "free" acidity was present but on two occasions the gastric contents became distinctly alkaline.



Case No. 7..... Magnesium Trisilicate Test.

Name..... Mr. G. S. ....

Age..... 28 ..... Date..... 3<sup>rd</sup> Dec. 1937 .....Diagnosis..... Rheumatoid Arthritis .....

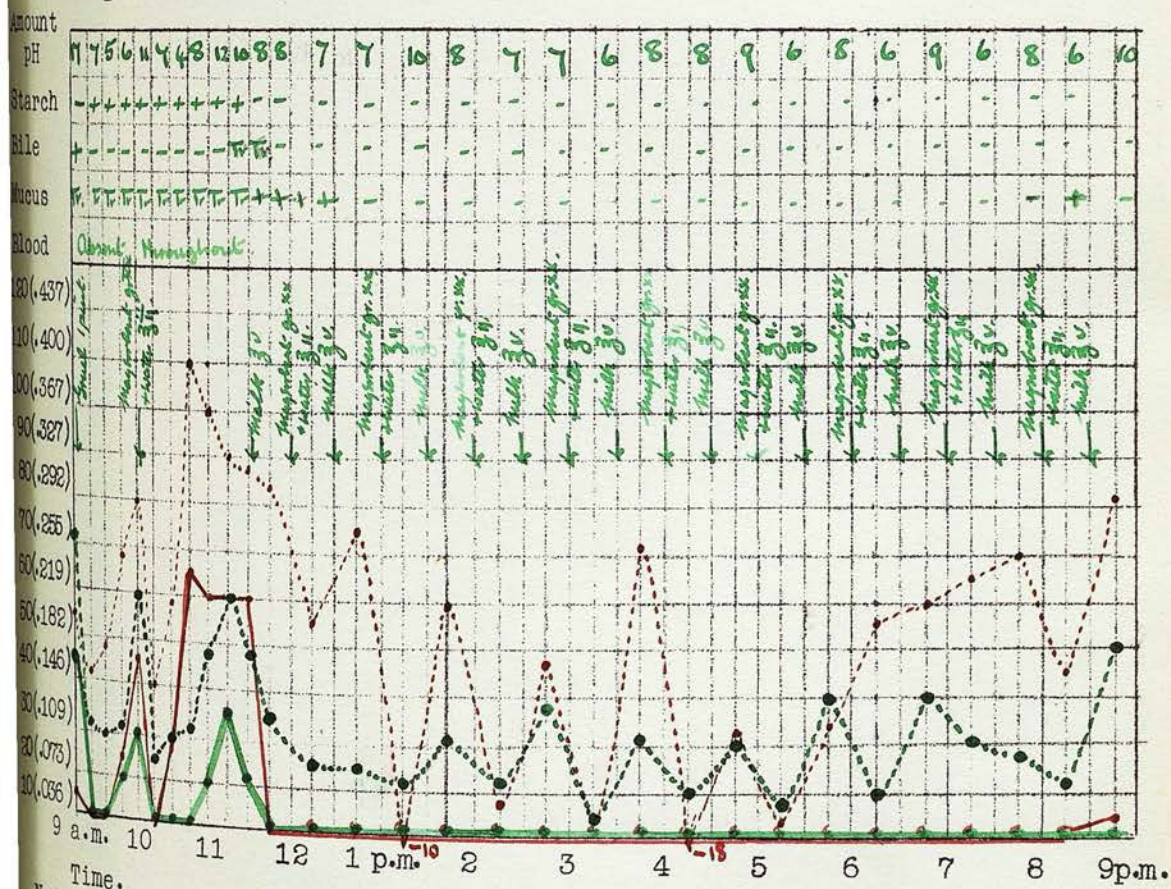
Substances given:-  
 A. "Food". 1). Bruil - 1 pint - at 9 a.m.  
 2). Milk - 5 oz. - at noon and hourly thereafter  
 B. Antacid(s). Magnesium Trisilicate ("Magerbent") - gr. xx  
in water 3 fl at 9.30 a.m., 12.30 p.m. and hourly thereafter.

Fasting juice. Amount..... 17..... c.c.  
 Special Characters.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



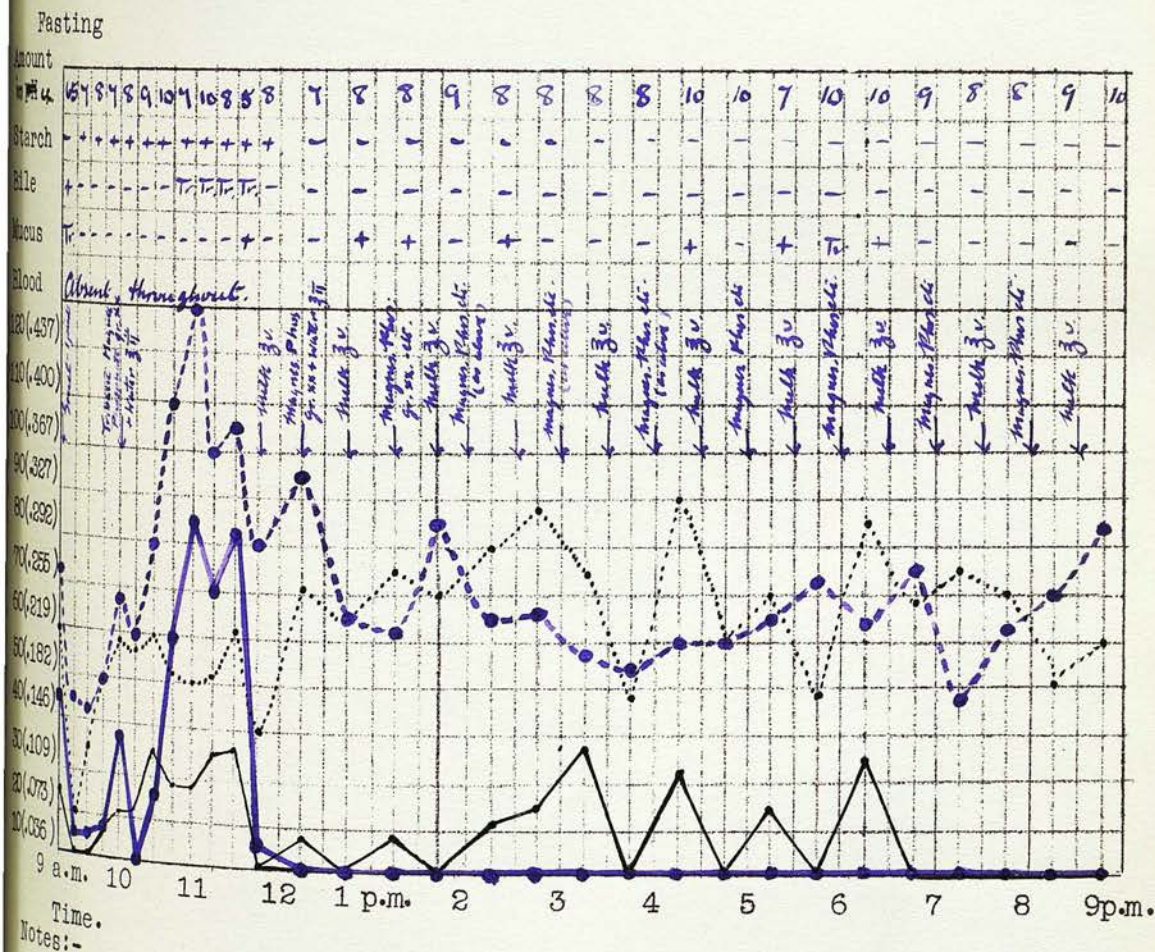
Notes:- This shows the favourable action of Magnesium Trisilicate when compared with the Sippy Powder, for there was more effective neutralisation with no evidence of a secondary acid stimulant action.

In the second part of the test there was no excessive action of the former powder which, theoretically, cannot cause an alkaline reaction in the stomach contents. Thus in this test it would appear to be a more effective and "physiological" antacid.



Case No. 27.....  
 Name Serge Sorbie.....  
 Age 28..... Date 6<sup>th</sup> Dec. 1937.....  
 Diagnosis Rheumatoid Arthritis.....  
 Substances given:- 1) Gruel 1 pint - at 9 am.  
 A. "Food". 2) Milk - 5oz. at noon & hourly thereafter.  
 B. Antacid(s) Tribasic Magnesium Phosphate - gr. xx in water 2oz.  
 at 9.30 am. and 12.30 pm. and hourly thereafter.  
 Fasting juice. Amount..... 65..... c.c.  
 Special Characters.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.  
 ..... represents total acidity.



Shows the very transient action of this antacid which was followed by the highest secondary stimulation of the three antacids tested.

During the second part of the test complete neutralisation of the small amount of "free" acid remaining was achieved without producing an alkaline reaction in the stomach contents.



## CASE NO. 8.

Miss A. McP.

Aged 61.

Complaint. "pain in the stomach", with no definite relation to the taking of food.

Duration. Almost continuous for 7 years.

Examination. Slight epigastric tenderness; she appeared emaciated from lack of food.

Barium Series - negative.

Cholecystography - " "

Fractional Test Meal - see chart.

Diagnosis. "Chronic Gastritis."

RESULTS OF GASTRIC CONTENTS' ANALYSES. (SUMMARY).

I. Effect of antacids on acid response to three-hour gruel test meals.

The control was persistently <sup>a</sup>slightly higher ~~than~~ normal. Magnesium Trisilicate gr.xx. neutralised this acid almost completely for the  $2\frac{1}{2}$  hours tested. Sippy No. 1 gr.xx. controlled the acid for 30 to 40 minutes, but this was followed by acid secretion which slightly exceeded that of the control. Tribasic Magnesium Phosphate gr.xx. controlled the acidity for 30 minutes, subsequent secretion being less than in the control.

II. Effect of antacids, (ever 9 hour period), on acid remaining after 5oz. hourly milk feeds.

The control showed the excellent antacid effect of these large frequent milk feeds on a case of slightly raised acid secretion; little free acid remained, but this was completely neutralised by all three of the above antacids in gr.xx. doses hourly.



Case No. **5... CONTROL TEST. (TEST WITH MAGNESIUM TRISILICATE- GREEN.**Name... **Miss. McPherson.**.....Age... **61**..... Date... **29<sup>th</sup> Nov. 1937**.....Diagnosis... **Chronic Gastritis**.....

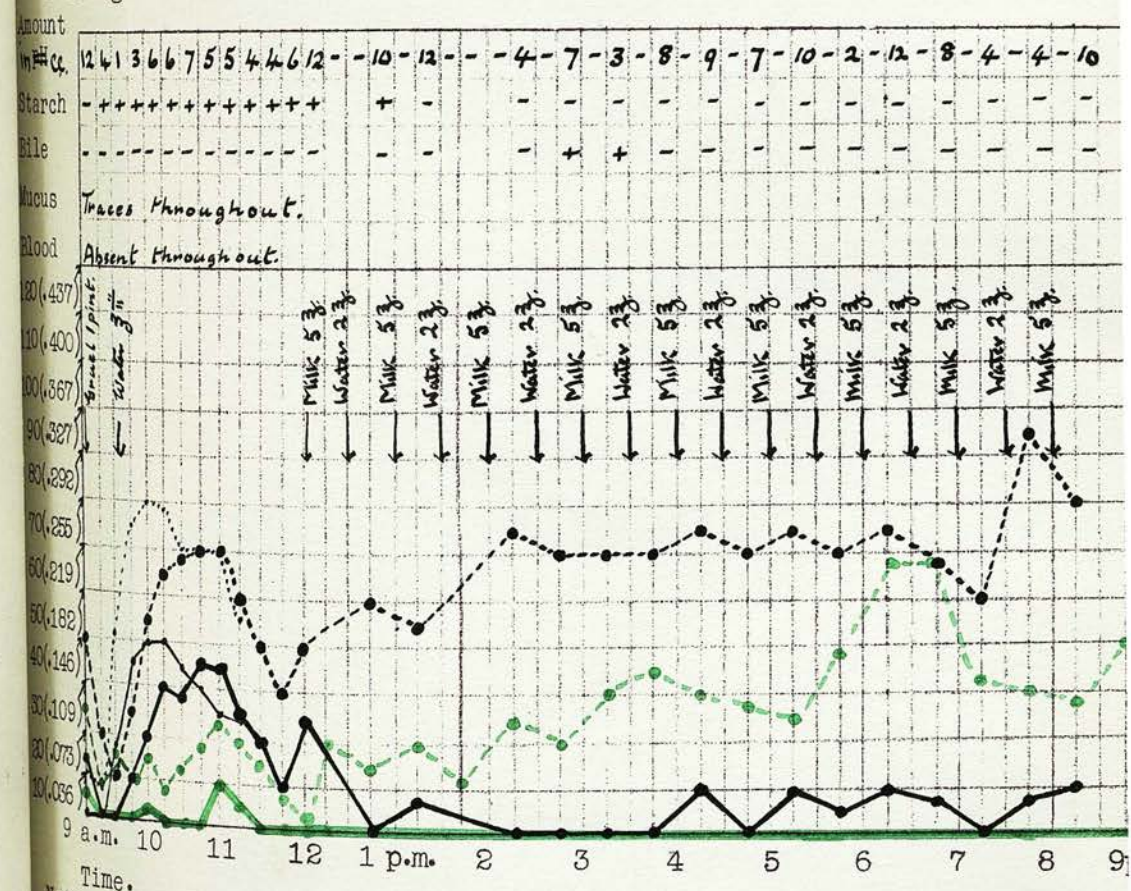
Substances given:-  
 1.) Gruel - 1 pint - at 9 a.m.  
 A. "Food". 2.) Milk - 5oz. at noon and water 2oz at 12.30,  
 B. Antacid(s). ..... and repeated hourly as indicated.

Fasting juice. Amount..... **1.2**..... c.c.  
 Special Characters.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- Double initial control curves show result of previous test meal when acid values were slightly higher.

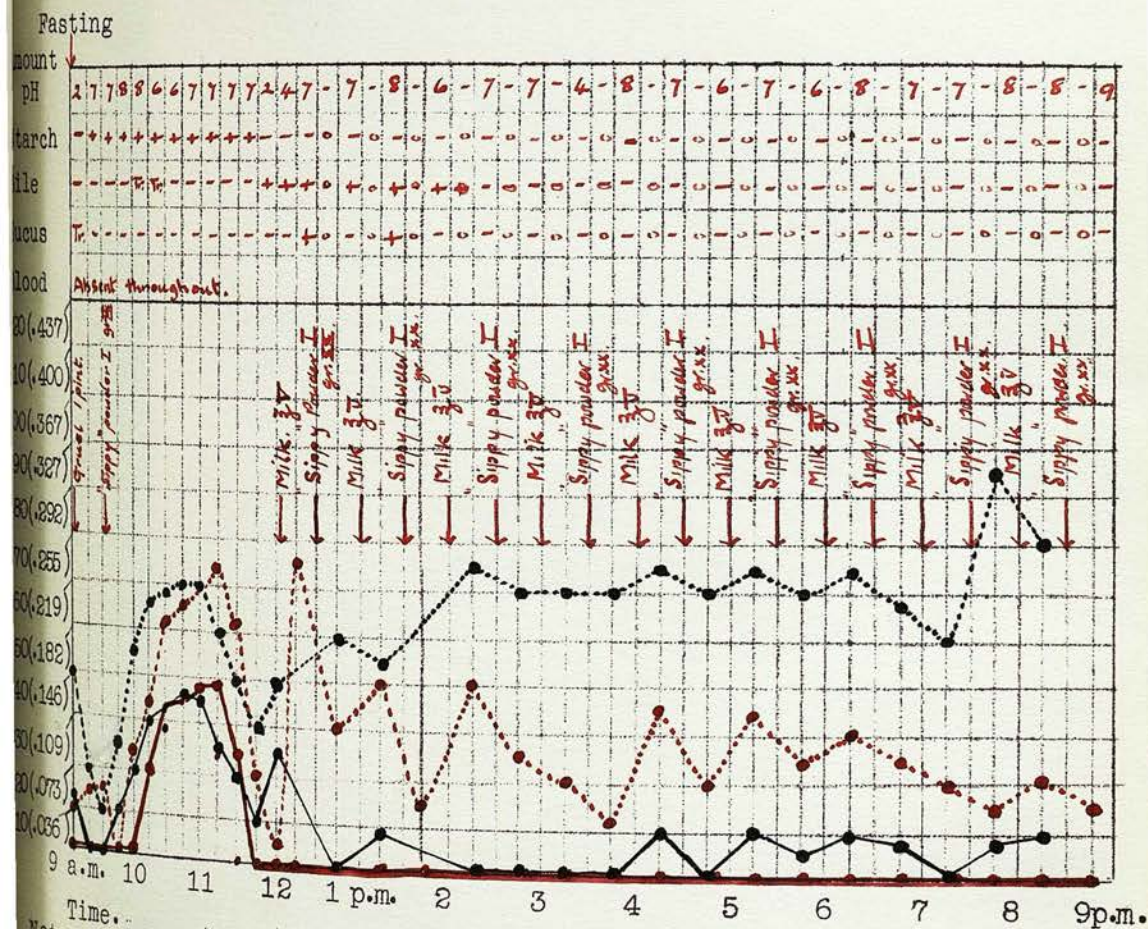
Control shows only slightly raised acid values on both occasions. The delay in the disappearance of starch suggests some pylorospasm which was probably responsible for some pain. Excellent antacid qualities of milk illustrated. Magnesium Trisilicate's admirable control of the acidity shown with no excessive neutralising effect, and no tendency to produce a secondary stimulation of acid secretion within the  $2\frac{1}{2}$  hours following administration of gr. xx.



Case No. S.I. SIPPY. NO. I. TEST. (CONTROL IN BLACK.)Name... Miss. McPherson.Date... 1<sup>st</sup> Dec. 1937.Diagnosis... "CHRONIC GASTRITIS"Substances given:- Gruel 1 pint (9 a.m.) + Milk 5oz. hourly from noon.A. "Food". SIPPY. NO. I. GR. XX. -as indicated.Fasting juice. Amount... 2. c.c.  
Special Characters... ---  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.



Notes:- Control shown in black: — = Free HCl, ..... = Total Acidity.

Shows 30 to 45 minutes neutralising effect followed by secondary acid stimulation greater than in control.

Complete control of acidity when given with milk feeds; no production of alkaline reaction at any time;

No significant effect on motility of stomach or pylorus; spasm, but subjective improvement noted.



Case No. 8. MAGNESIUM TRISILICATE TEST. (SIPPY NO. I. IN RED.)

Name Miss McPherson

Age 61 Date 3rd Dec. 1937

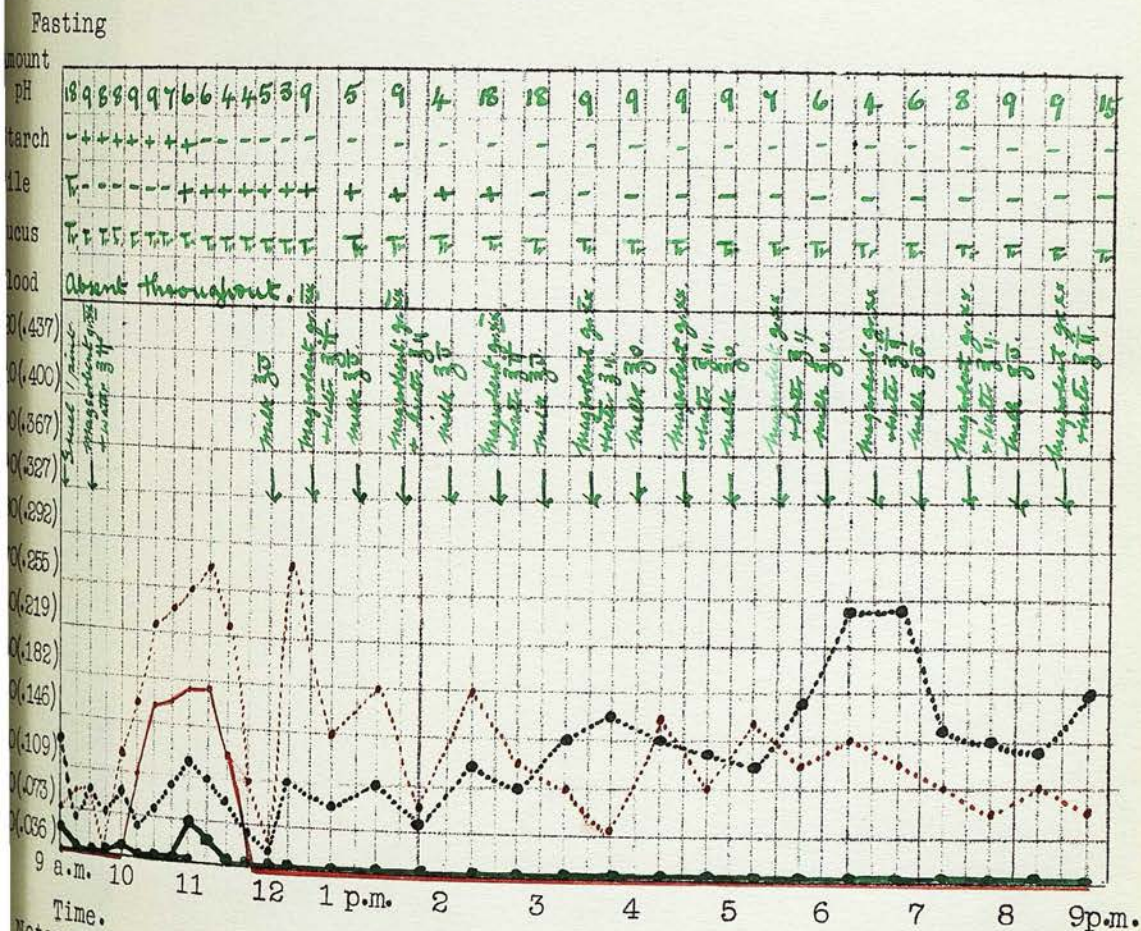
Diagnosis "CHRONIC GASTRITIS."

Substances given:-  
 1.) Gruel - 1 pint - at 9 a.m.  
 2.) Milk - 5oz at noon, and hourly thereafter.  
 B. Antacid(s). Magnesium Trisilicate (Magsorbent) gr. xx  
 in water  $\frac{3}{4}$  at 9.30 a.m., 12.30 p.m., and hourly thereafter.

Fasting juice. Amount 18 c.c.  
 Special Characters  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.





Case No. 8. TRIBASIC MAGNESIUM PHOSPHATE TEST. (CONTROL.) BLACK, )...Name Miss McPherson.....Age 61..... Date 6<sup>th</sup> Dec. 1937.....Diagnosis "Chronic Gastritis".....Substances given:- "1) Gruel - 1 pint at 9am.A. "Food". 2.) Milk - 5oz at noon, and hourly thereafter.B. Antacid (9) Tribasic Magnesium Phosphate gr. xx in

Fasting juice. Amount..... c.c.

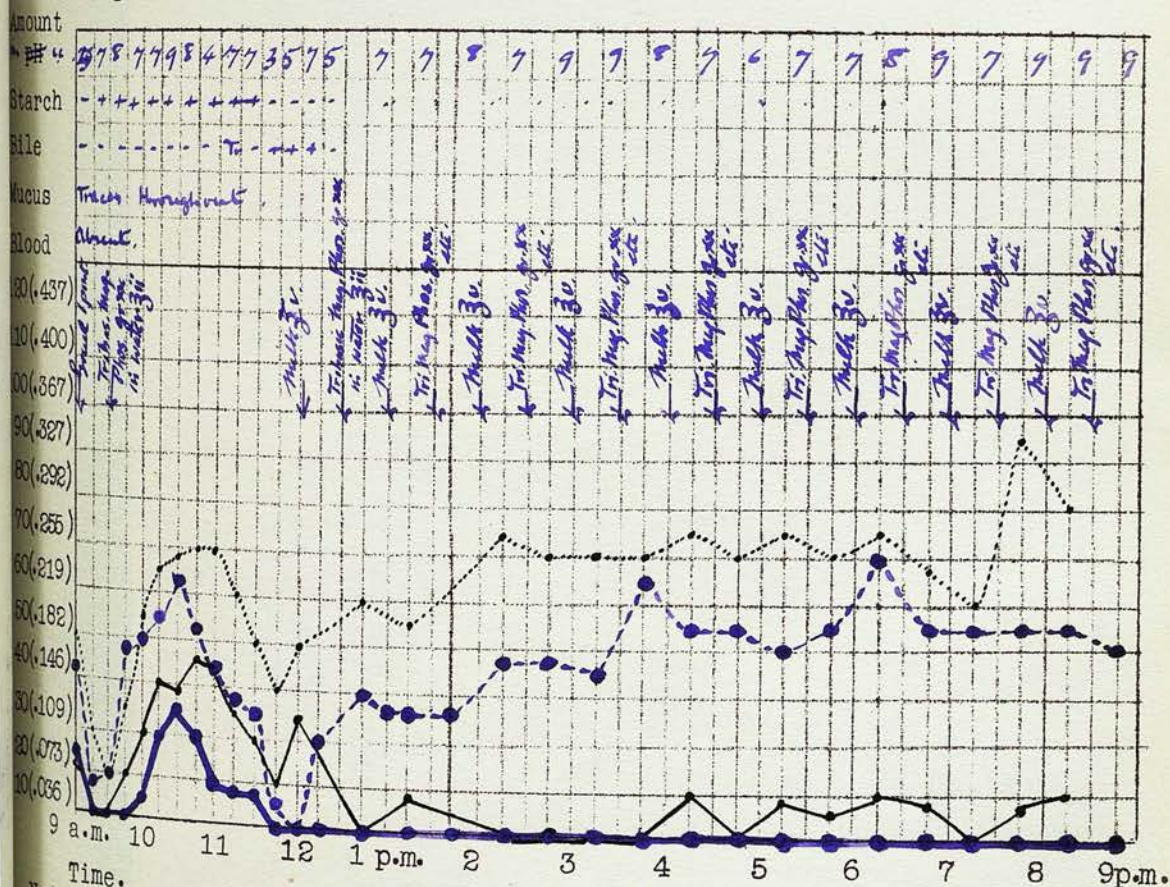
Special Characters.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting





## CASE NO. 9.

MISS C. B.

Aged 18.

Complaint. Epi gastric pain and vomiting - 1 day.

Examination. Clinically - negative.

Test Meal - within normal limits.

Faeces - no occult blood.

Barium Series- negative .

Diagnosis. "Acute Gastritis, due to dietetic error."

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

I. Effect of antacids on three hour test meal.

"High normal" acidity of the control was not greatly influenced by any of the three powders given in 2ogr. doses immediately after the gruel.

Magnesium Trisilicate kept the acid low for about 45 minutes, but the average over the three hours was higher than the control. Sippy Powder No. I. had an even poorer effect. Tribasic Magnesium Phosphate was effective for 30 minutes longer, but even here the acidity subsequently rose slightly higher than the control.

II. Effect of antacids on nine hour test with 4oz. hourly milk feeds.

Control shows moderate acidity which was completely controlled by Tribasic Magnesium Phosphate in 2ogr. doses between the milk feeds. Almost complete neutralisation was achieved with the Sippy Powders. Magnesium Trisilicate being only slightly better than the milk feeds alone as given in the control.



Case No. 9.....

Name..... Miss. C. BREMNER.....

Age..... 18..... Date..... 7th Dec. 1937.....

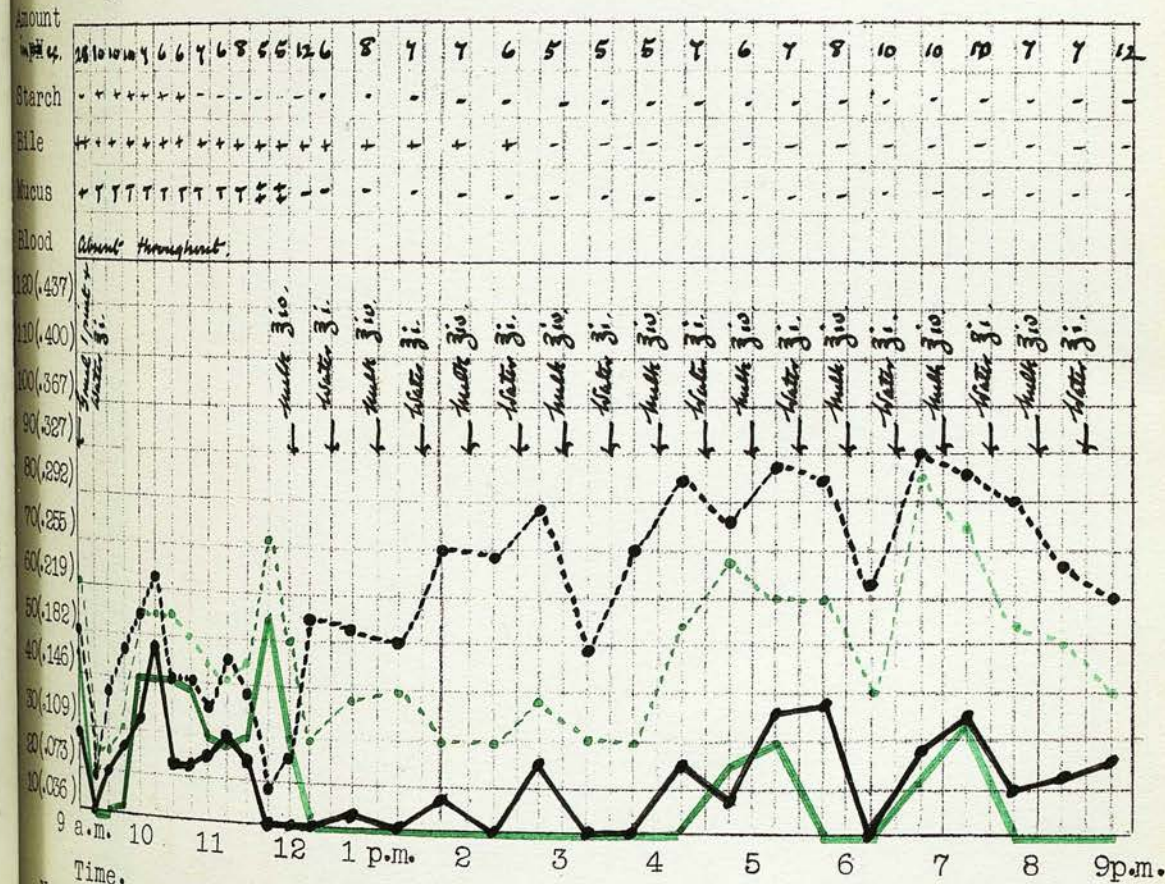
Diagnosis..... Acute Gastritis.....

Substances given:-  
A. "Food". *Bread 1 pint + Water 1 1/2 pt. at 9 am.*B. Antacid(s). *Milk 3 oz. at noon, and hourly thereafter.  
Water 3 oz. at 12.30 pm. "*Fasting juice. Amount..... 25..... c.c.  
Special Characters.....  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



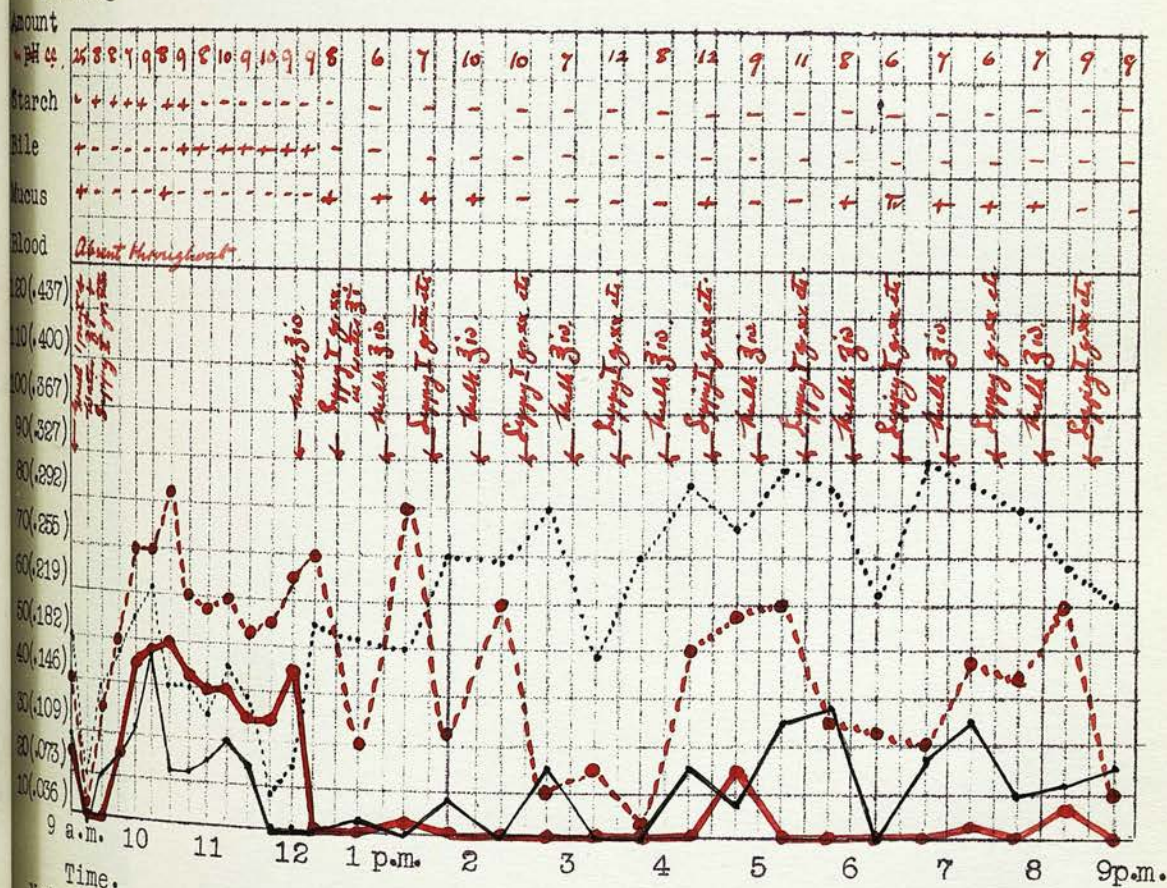
Notes:-

A case of "high normal" acidity; acidity is on the whole well controlled by the milk feeds never reaching 30 points.

The corresponding test with Magnesium Trisilicate shows that after a short period of acid control acidity soon reached level which was on the whole higher than that of the control. In the second part of the test the powder achieved little improvement on the control result.



## Fasting



Notes:-

There was a transient neutralising effect followed by a secondary rise in acidity which lasted throughout the remainder of the test .

In the second part of the test the Sippy Powders achieved almost complete control of the low acidity present in the control.



Case No. .... 9. ....

Name..... Miss C. BREMNER .....

Age..... 18. .... Date..... 11th. Dec. 1937. ....

Diagnosis..... Acute Gastritis. ....

Substances given:-

A. "Food". *Break 1 pint. at 9am. + milk 3/4 at noon + hourly thereafter.*B. Antacid(s). *Magnesium Trisilicate gr. xx in water 3/4 at 9am. at 12.30 pm. and hourly thereafter.*

Fasting juice. Amount..... 18. .... c.c.

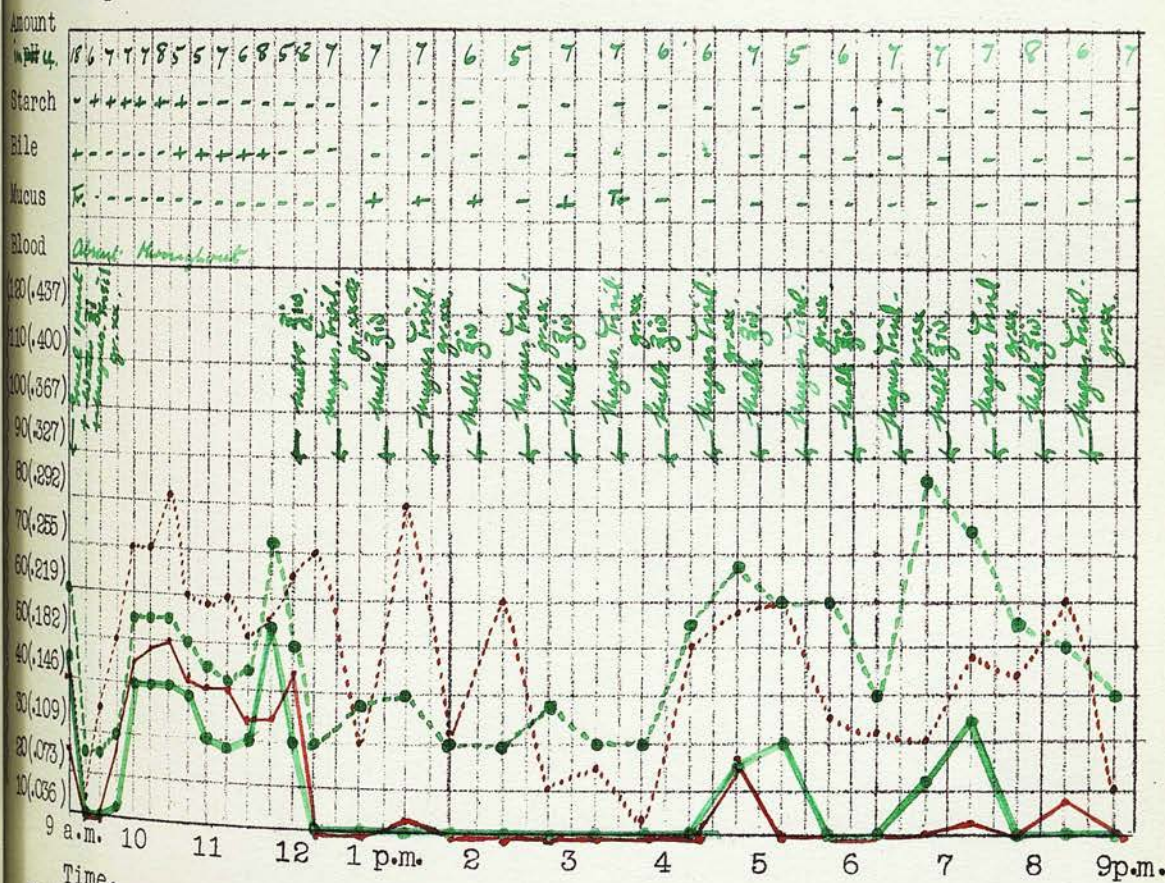
Special Characters.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- The effect of Magnesium Trisilicate is shown to be a little more prolonged than that of the Sippy Powders in the first part of the test (The rise at the end of the three hours is probably not due to the Magnesium Trisilicate).

With the milk feeds this powder was the least satisfactory of the three tested, and, indeed, the result was little better than with milk alone.



Case No. 9.....  
 Name Miss C. BRAMNER.....  
 Age 18..... Date 13th Dec 1937.....  
 Diagnosis Acute Gastritis.....

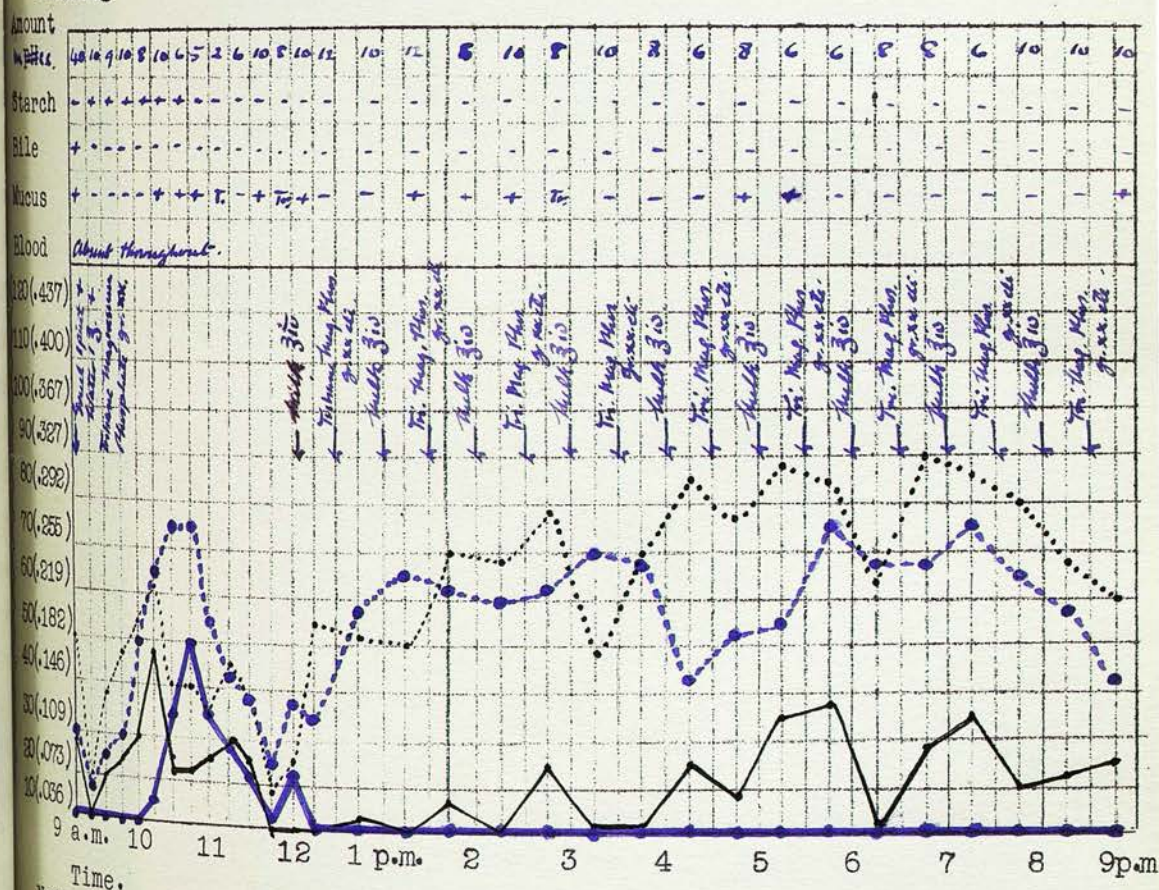
Substances given:-  
 A. "Food" Gruel (1 pint) at 9 a.m. + milk 3 1/2 at noon & hourly thereafter.  
 B. Antacid (8) Tribasic Magnesium Phosphate gr. 1/2 in water 3 1/2  
at 9 a.m., 12.30 p.m. and hourly thereafter.

Fasting juice. Amount 40..... c.c.  
 Special Characters.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- This chart shows the satisfactory effect of Tribasic Magnesium Phosphate in controlling the "free" acidity for over one hour without the production of any definite secondary rise in acidity.

Complete control was maintained throughout the second part of the test.



CASE NO. ~~10~~ 10.

MR. S. H.

Aged 31.

Complaints. Asthma 27 years.  
 Epigastric pain 3 months.  
 Haematemesis on day of admission.

Examination. Epigastric tenderness; emaciation.

Test Meal - see chart.

Barium Series -(after 3 weeks treatment)-

"Negative for ulcer- stomach low and  
 atonic."

Diagnosis. Duodenal Ulcer.

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

## I. Effect of antacids on gruel test meal (3 hour).

In this case of moderate hyperacidity Sippy No. I.  
gr. xx. controlled the acid for 60 to 75 minutes, pro-  
 ducing an alkaline reaction, but no marked secondary  
 rise. Magnesium Trisilicate and Tribasic Magnesium  
Phosphate results show a 15 to 30 minute neutralisa-  
 tion and again lower values throughout the period of  
 the test with no overpassing of the neutral point.

## II. Effect of antacids hourly (9 hour test) along

With 3oz. milk feeds hourly.

Values with Sippy powder varied between plus 50 points  
 and minus 18; on the whole it was unsatisfactory.

Magnesium Trisilicate produced almost complete neut-  
 ralisation throughout the 9 hours.

Tribasic Magnesium Phosphate's effect was less satis-  
 factory than that of the control; during the latter  
 acid was present practically continuously, and rose to  
 over 40 points on several occasions.



se No. 10. CONTROL (BLACK), WITH MAGNESIUM TRISILICATE TEST.

MR. S. H. Date 21st. Dec. 1937.

Diagnosis.....Dordanal. Ulcer. (Haematemesis.)

Substances given:- Gruel I pint :milk 3oz. -as indicated.

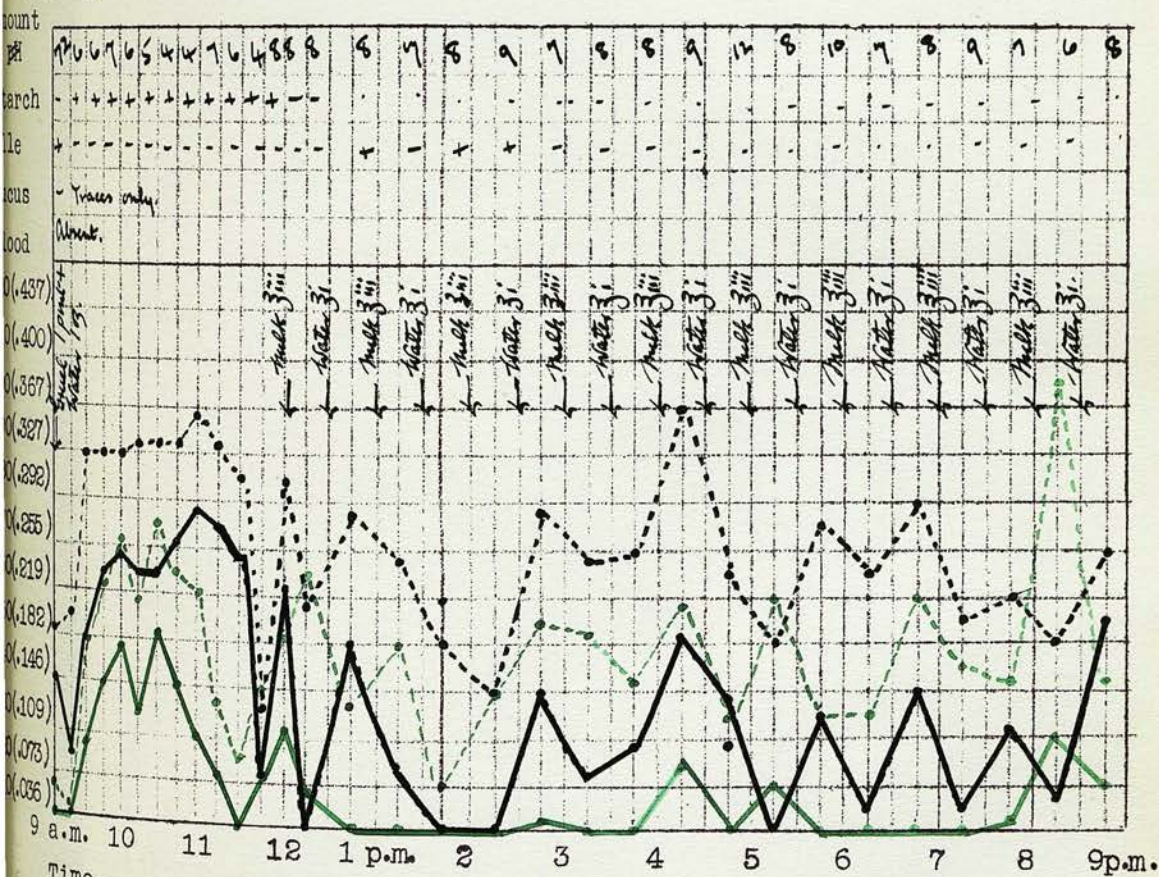
A. "Food". ..None..Water. 1oz..-as indicated.

Stomach juice. Amount.....72..... c.c.  
Special Characters...none.....  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Control shows a hyperacidity type of response which was not well controlled by the milk feeds, "free" acid rarely falling to nil and on three occasions attaining 40 points. The sudden fall in acidity in the 11th specimen may have been due to cessation of secretion by the stomach, for only a small specimen was with difficulty obtained, and this seemed to consist mainly of saliva: the acid value had again risen in the 12th specimen, but it is probable that there was little secretion in the stomach, and this was easily neutralised by the small milk feed.

The initial acidity was low on the day on which Magnesium Trisilicate was given, but the subsequent lower acid values must be attributed in some small measure to it; certainly, with milk feeds, the result was almost complete acid control.



Case No. 10. SIPPY NO. I. POWDER TEST. (CONTROL. - BLACK.)

Name..... MR. S. H. ....

Age..... 31..... Date..... 27th Dec 1937.....

Diagnosis..... Duodenal Ulcer. (Haematemesis.) .....

Substances given:- Gruel - I pint; milk 3oz. - as indicated.

A. "Food". .....

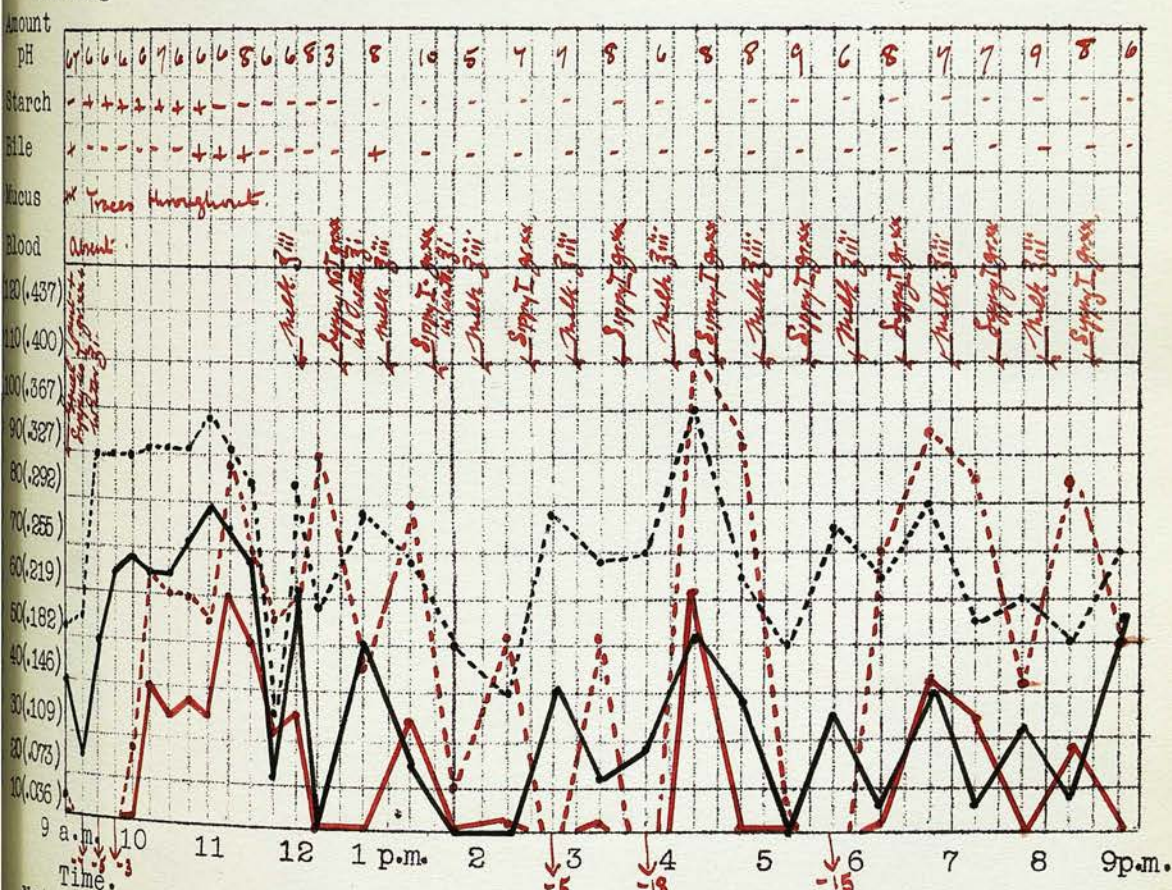
B. Antacid(s). Sippy No. I. gr. xx. in water. 1oz. - as indicated.

Fasting juice. Amount..... 67..... c.c.  
Special Characters..... none.....  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- The initial low acid content of the fasting juice on this day might indicate that lower values would have been obtained had the control been done on this day, but consideration of the other tests in the series suggests that this is by no means certain.

Given after the gruel, the powder controlled the acid for over one hour, and subsequent values remained below those of the control. A distinctly alkaline reaction had been produced.

During the remainder of the test the undesirable effects of this powder are well illustrated, for, although gastric acidity was kept at a low level for considerable periods, the stomach contents became alkaline on three occasions; this probably stimulated acid secretion, high values (e.g. 50 points) being obtained. Emptying time appears accelerated by about  $1\frac{1}{4}$  hours.



Case No. 10. MAGNESIUM TRISILICATE TEST (GREEN). SIPPY NO. I. (RED).

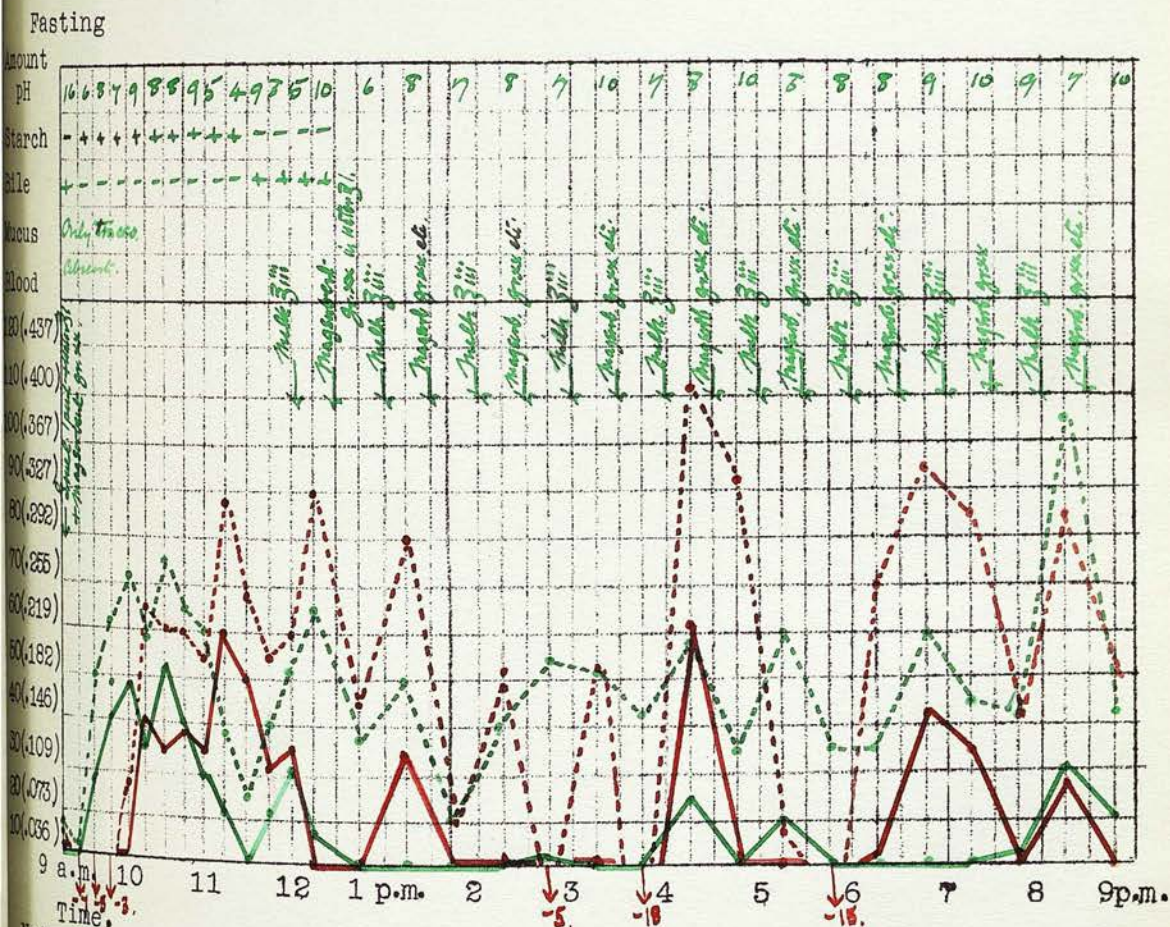
Name..... MR. S. H. ....  
 Age..... 31..... Date... 29th Dec. 1937.....  
 Diagnosis..... Duodenal Ulcer. (Haematemesis.) .....

Substances given:- Gruel - I pint ; milk 3oz. - as indicated.  
 A. "Food". Magnesium Trisilicate gr. xx. in water 1oz.  
 B. Antacid(s) -as indicated.

Fasting juice. Amount..... 16..... c.c.  
 Special Characters..... none.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.



Notes:- This chart shows well the advantages of Magnesium Trisilicate over Sippy Powder No. I. Although the single small dose was not so effective in dealing with the acid, yet no alkaline reaction was produced and the acid did not afterwards rise to quite so high a level.

With the help of the small milk feeds Magnesium Trisilicate was almost successful in neutralising the acid throughout the day, and at no time did the acid rise to a level which, one believes, would materially affect the healing of an ulcer or produce symptoms; the neutral point could not be overpassed. Emptying time was apparently diminished by about  $\frac{5}{4}$  hour.



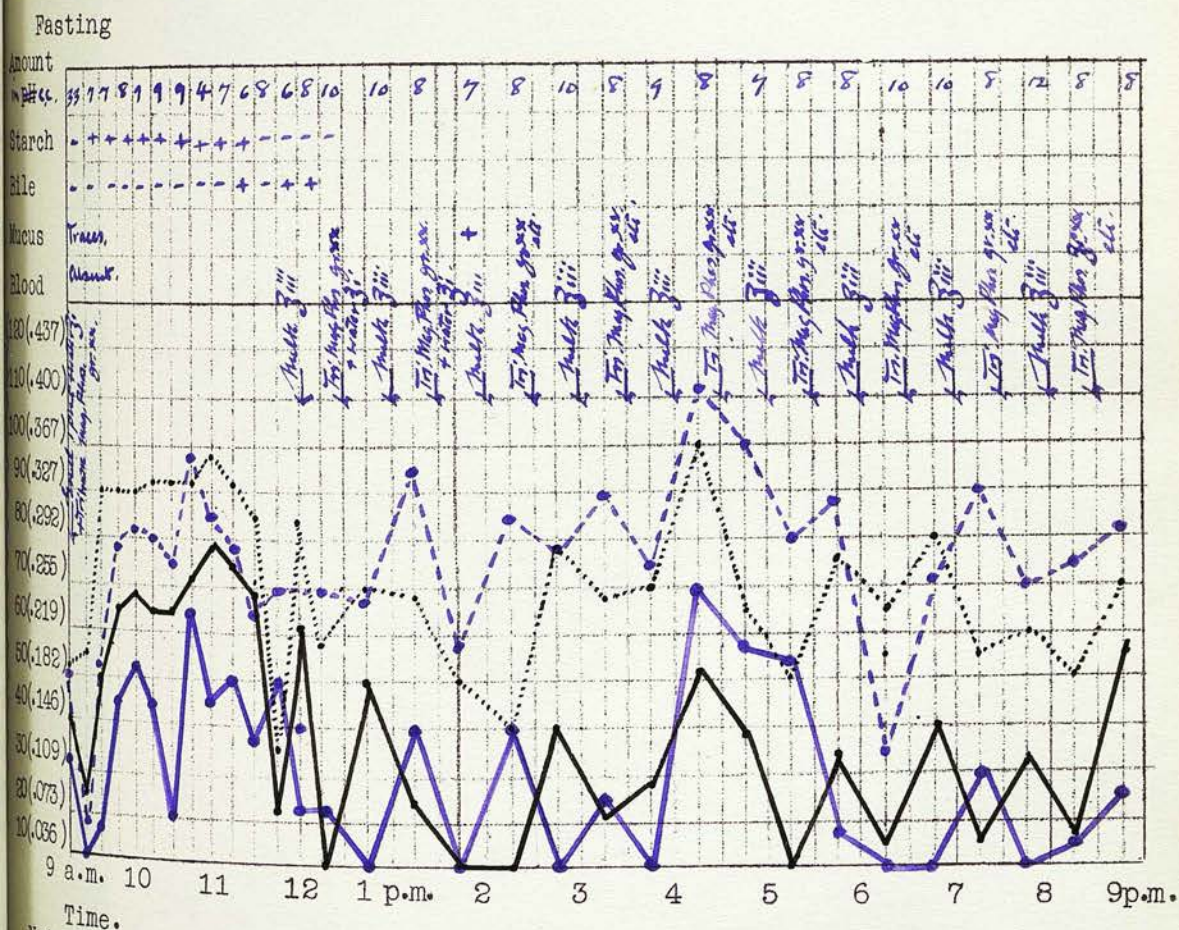
Case No. 10... TRIBASIC MAGNESIUM PHOSPHATE TEST. (PURPLE).  
MR. S. H.

Name.....  
Age..... 31..... Date... 23rd. Dec. 1937.....  
Diagnosis..... Duodenal Ulcer. (Haematesis.).....

Substances given:- Gruel-1 pint; milk 3oz.-as indicated.  
A. "Food".  
B. Antacid(s). Tribasic Magnesium Phosphate gr. xx.  
in water 1oz. -as indicated.  
Fasting juice. Amount..... 33..... c.c.  
Special Characters..... none.....  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.



Notes:- Effect of single dose similar to but slightly less effective than Magnesium Trisilicate.

This antacid is distinctly the least effective of the three tested in controlling gastric acidity throughout the day, and milk alone as in the control would appear to be better.



## CASE NO. II.

MR. G.W.

Aged - 31.

Complaint. Severe epigastric pain with passage of black motions for 24 hours before admission.

Examination. Some epigastric tenderness on day of admission, but nil else clinically.

Stools - persistently negative Benzedine Test.

Test meal - discussed in charts.

Barium series - negative.

Diagnosis. "Hyperchlorhydria".?Acute peptic ulcer.

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

**I. Effect of antacids on three hour test meal.**

Transient hyperacidity of control was not favourably affected by any of the three antacids tested and given after the gruel meal.

Magnesium Trisilicate was a poor best; there was a "delayed" antacid effect, and no marked stimulation.

Sippy powder showed a transient effect followed secondary stimulation of acid exceeding the control.

Tribasic Magnesium Phosphate result showed a low acidity for some 45 minutes following ingestion, but this was at once offset by greater and more prolonged acid stimulation than in the cases of the other two.

**II. Effect of antacids on acidity of nine hour test with hourly 3oz. milk feeds.**

Control showed considerable acidity which was effectively neutralised by all three antacids; Sippy NO. I. however produced a distinctly alkaline reaction twice.



Use No. 11. CONTROL TEST. (MAGNESIUM TRISILICATE TEST IN GREEN).

MR. G. WAHNSSTROM.....

Date 13th. Dec. 1937.....

PT. ....

Diagnosis "Hyperchlorhydria" ? Acute. Peptic. Ulcer....

Substances given: - Grue? - 1 pint (9am.) + Water 3i

A. "Food" Milk 3iv at noon and hourly thereafter.

B. Antacid(s) Water 3i at 12.30 pm and hourly thereafter.

Fastest juice. Amount 52..... c.c.

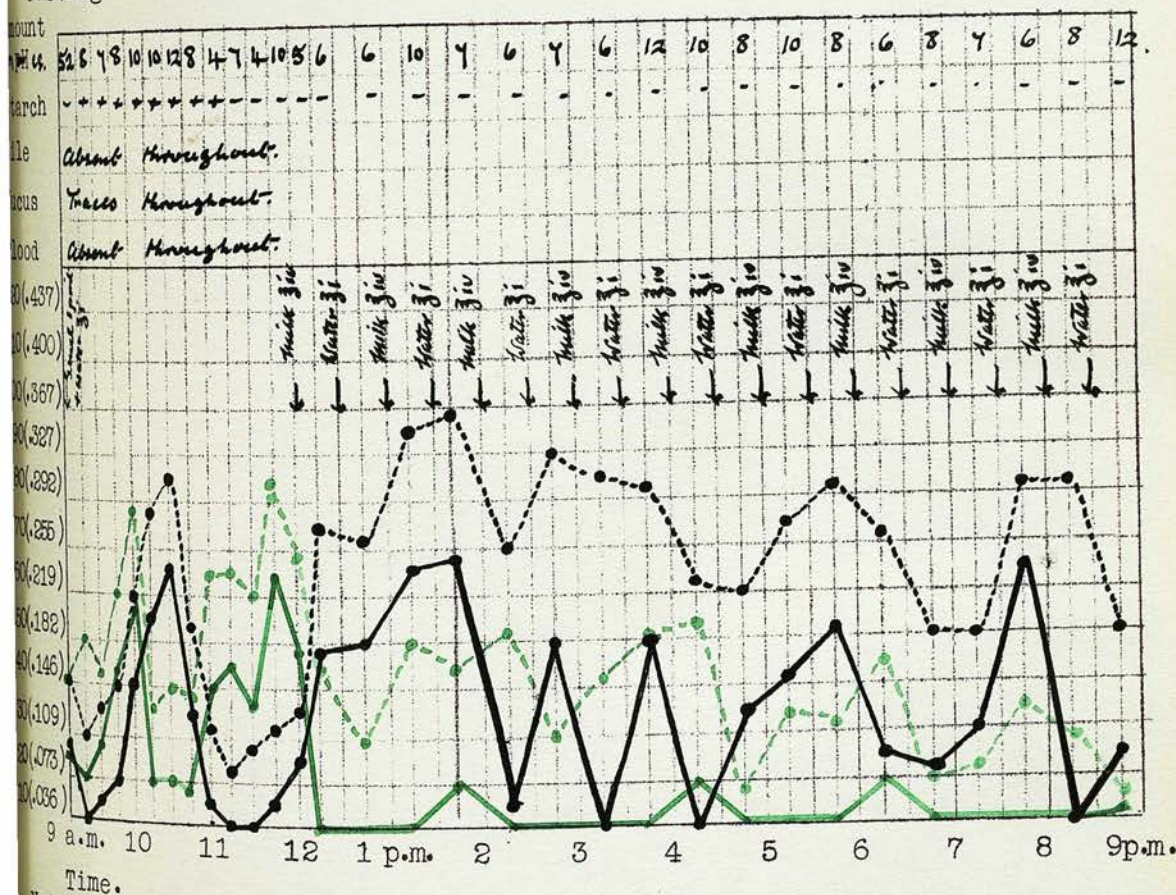
Special Characters.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes: - Control shows transient hyperacidity after gruel test. Milk feeds quite unsuccessful in combating the acid response they provoke.

No definite evidence of pylorospasm.

Initial effect of Magnesium Trisilicate apparently insignificant, but acid values on the whole lower than control. Is remarkable fall in acidity  $1\frac{1}{4}$  hours after taking powder due to its effect not having reached that portion of the gastric contents from which specimens were being taken, or could it possibly be associated with long continued neutralising effect of this antacid on a diminishing acid secretion? The former explanation is almost certainly the correct one.

Note the very satisfactory, if not quite complete, acid control in the remaining portion of the test with milk.



Case No. **SIPPY NO. I. POWDER TEST (RED). CONTROL (BLACK).**

MR. G. WAHLSTROM.....

SI. .... Date... **18<sup>th</sup> Dec. 1937**.....

Diagnosis... **"HYPERCHLORHYDRIA" ? ACUTE PEPTIC ULCER**.....

Substances given:- **Food (1 pint at 9am): Milk 3iv at noon, and hourly thereafter.**

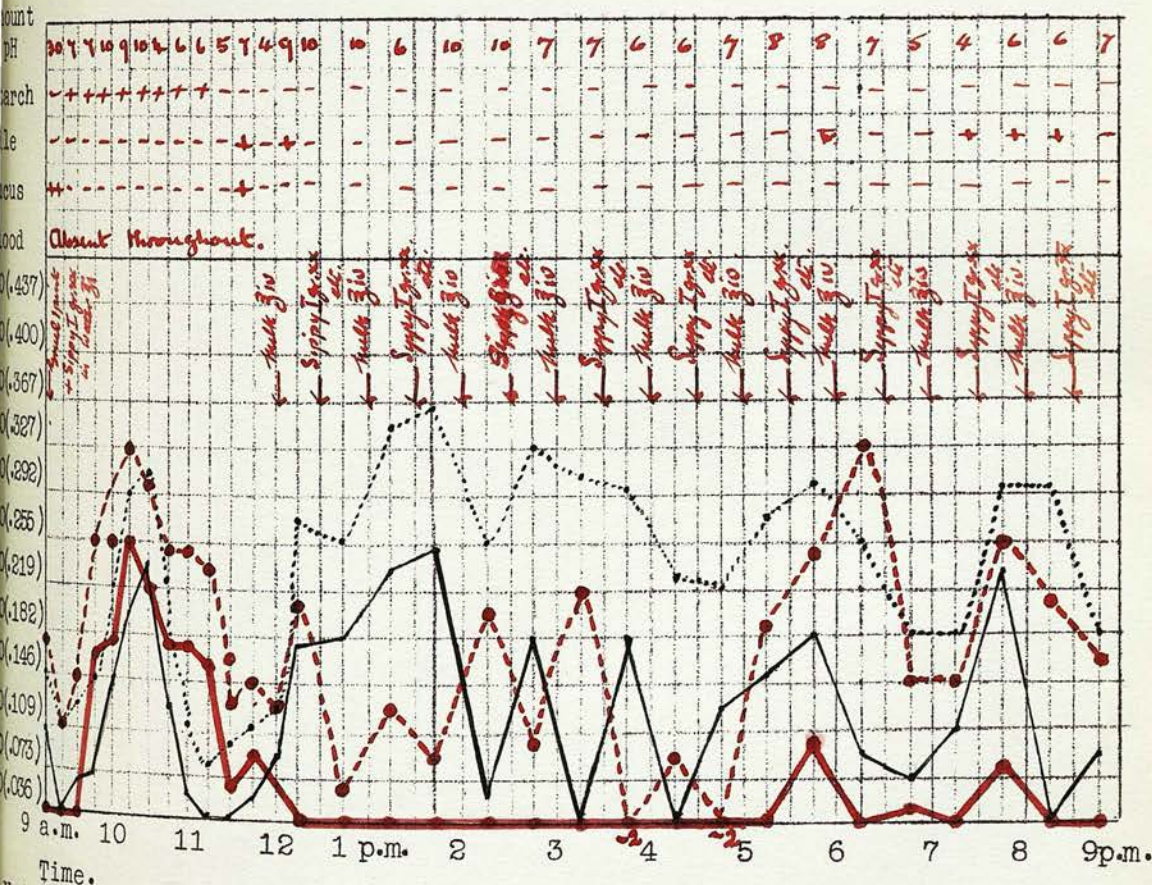
B. Antacid(s). **Sippy I. powder gr. xx at 9.5 am, 12.30 pm and hourly thereafter, (in water 3i).**

Stimulating juice. Amount..... **30**..... c.c.  
Special Characters..... **Mucus ++**.....  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- In first part of test acid rise delayed for about 30 minutes; this is followed by the usual secondary acid secretion which results from administration of these alkalis and which in this case is prolonged and exceeds the control.

Given hourly with the milk feeds the powder produces a good result except that the neutral point is passed on two occasions.



MR. G. WALSTROM.....Date 15th Dec. 1931.....

Diagnosis..... "HYPERCHLORHYDRIA." ?ACUTE PEPTIC ULCER....

Substances given:-

A. "Food". 3oz (1 pint - 9 am.) : Milk 3/10 at noon, and hourly thereafter.B. Antacid (8). Magnesium Trisilicate gr. XX - immediately after  
meal, & at 12.30 pm. and hourly thereafter.Fasting juice. Amount..... 35 cc...... c.c.

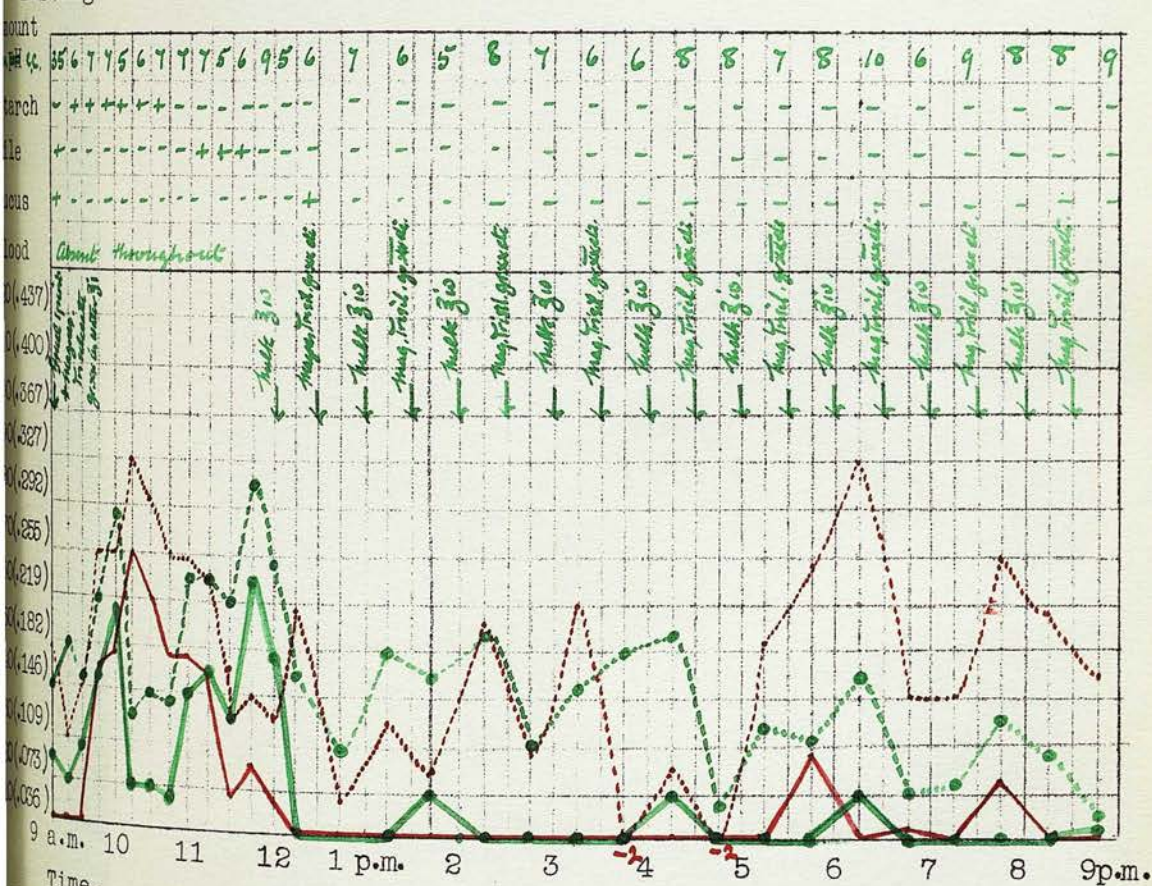
Special Characters.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- Shows initial slightly more efficient antacid effect of Sippy Powder offset by the secondary stimulant action of this combination of drugs; both results are transient.

There is little to choose between the two powders given hourly between the milk feeds, but Magnesium Trisilicate is to be considered the more satisfactory, since at no time did it reduce the reaction of the gastric contents below the neutral point. The high total acidity values in some cases with Sippy Powder probably indicate considerable acid secretion by the stomach in an effort to overcome the "unphysiological" alkalinity of its contents.



## CASE NO. 12.

MISS C.F.

Aged 53.

Complaint. Epigastric pain to the left of the mid-line, coming on one hour after food and relieved before the next meal. No remissions.

Duration. 12 years.

Examination. Clinically -nil to note.

Test meal - see special charts.

Radiologically:-

Barium Series - negative.

Barium Enema - " .

Diagnosis. "Hyperchlorhydria."

RESULTS OF GASTRIC CONTENTS' ANALYSES. (SUMMARY).

I. Effect of drugs on acid response to gruel test meal:-

Acid neutralised for 45 to 60 minutes after administration of gr.xx. Magnesium Trisilicate; no subsequent acid stimulant effect noted.

Acid neutralised for 15 to 30 minutes after same dose of Sippy Powder No.I., with subsequent rise in acidity to above control level.

Acid "neutralised" for 15 to 30 minutes by gr.xx. Tribasic Magnesium Phosphate, but effect was incomplete, and was followed by an even greater acid secretion than in the case of Sippy No.I.

Emptying time would appear to have been accelerated by one hour in the case of the Sippy Powder; no effect observed with the two others.



TRIBASIC MAGNESIUM PHOSPHATE TEST (PURPLE).

MR. G. WALHSTRÖM

No. 31. Date 20<sup>th</sup> December, 1937.  
 "HYPERCHLORHYDRIA." ?ACUTE PEPTIC ULCER.  
 Diagnosis.....

Substances given:-

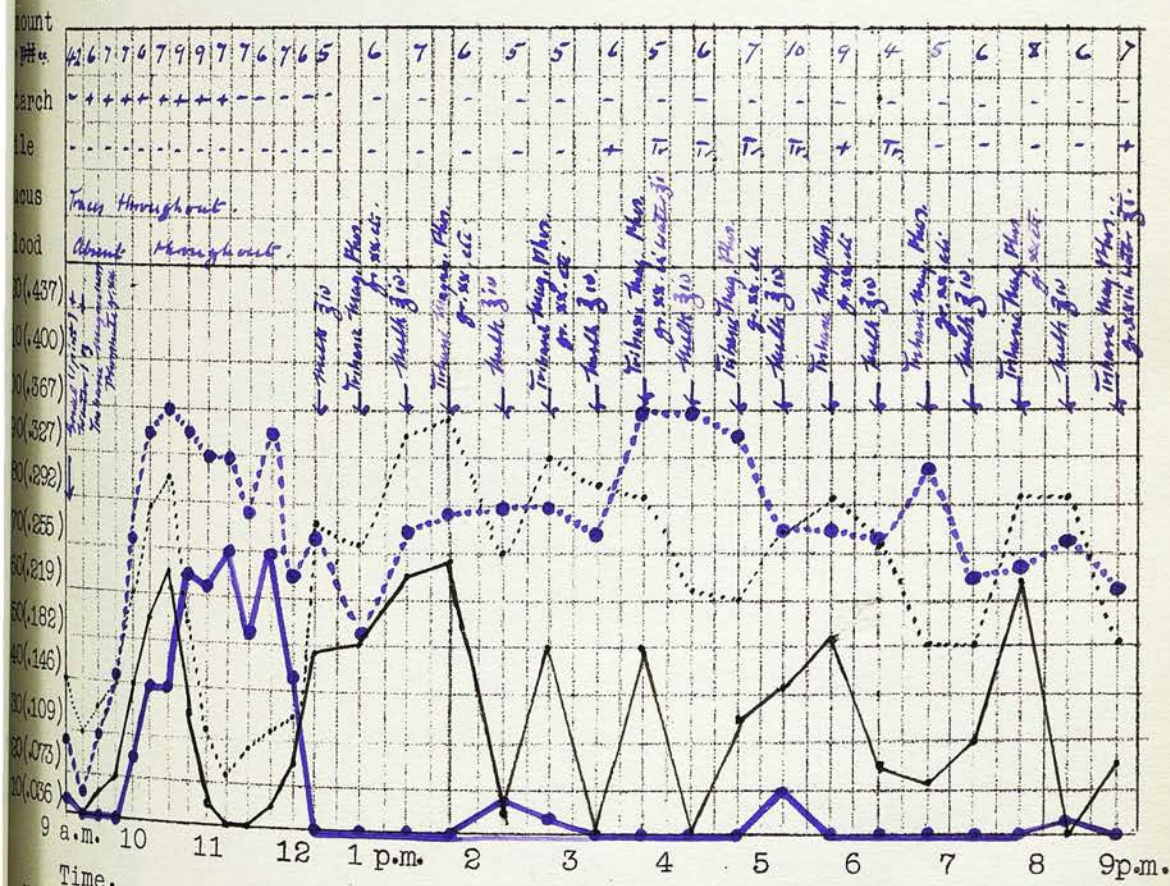
- A. "Food". *Small 1 pint (9 am.) Milk (3:10) 12 min. and hourly thereafter*  
 B. Antacid(s) *Trisilicic Magnesium Phosphate (gr. xx) in water 3i*  
*at 9 am., 12.30 pm. and hourly thereafter (v.i.)*

Stomach juice. Amount..... 42 c.c.  
 Special Characters.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- Acid was controlled for about 1 hour by initial single dose, but very marked secondary rise followed.

On this occasion this antacid was equal in efficiency to Magnesium Trisilicate in dealing with the acid in the second part of the test.

SUMMARY.(Miss C.F. Contd.).

II.Effect of antacid drugs on acidity remaining after hourly 3oz. milk feeds.

Magnesium Trisilicate and Sippy No.I. in gr.xx. doses both very effective, but the former if any- the better since the acid was more quickly reduced, and the reaction of the gastric contents never became alkaline.

Tribasic Magnesium Phosphate was somewhat less effective than the other two.



No. 12.....

Miss F.

Date... 21 st. Dec. 1937...

"Hyperchlorhydria."

stances given:-

A. "Food". Milk (3oz.) and gruel (1 pint) -as indicated.

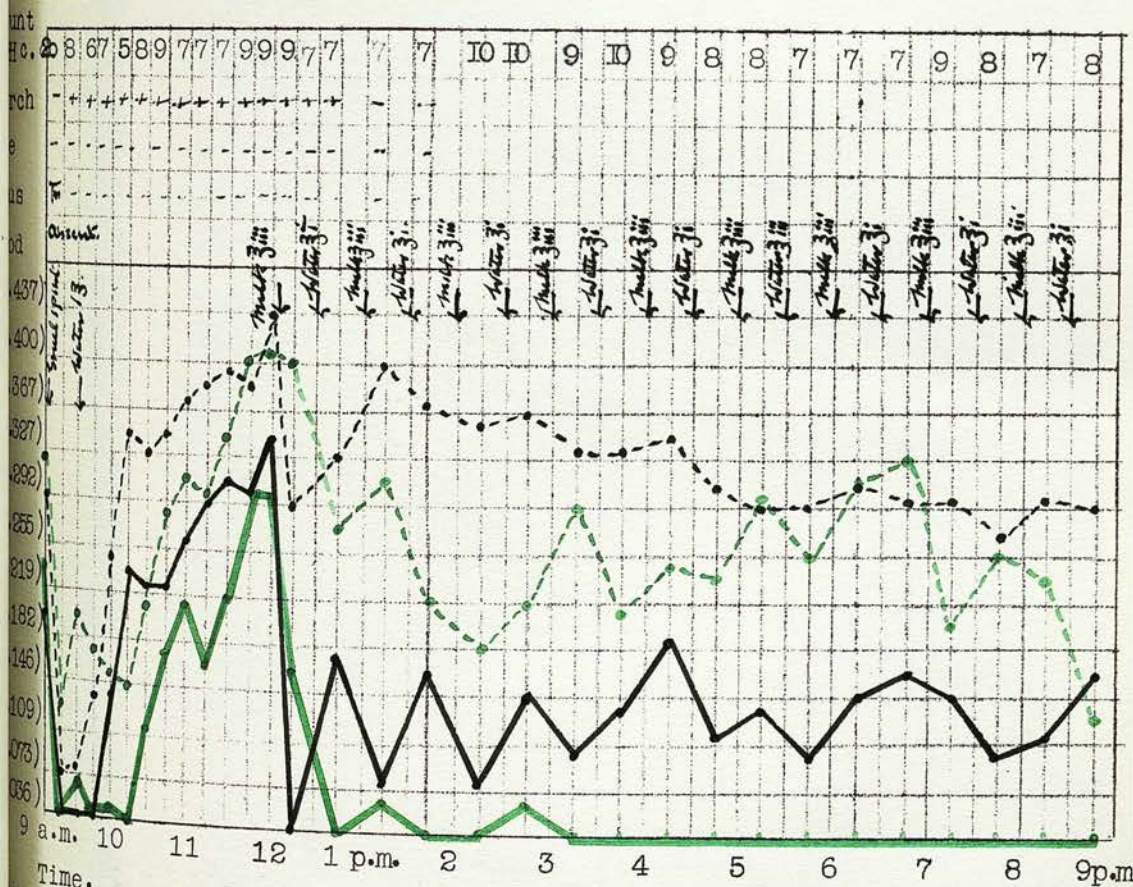
B. Antacid(s). None. Water 1oz. -as indicated.

ing juice. Amount..... 20 c.c.  
 Special Characters... none.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Time.  
 Notes:-

Corresponding test with Magnesium Trisilicate (green).

The control test shows a very high acidity with a "climbing" type of curve. This high "free" acid was completely neutralised by 3oz. of milk, due probably to there being only a small amount of highly acid secretion in the stomach, for the neutral point was never again attained throughout the day despite milk feeds of 3oz. hourly. High acid readings were often obtained during this period, e.g. 42 points, especially just before the next feed was due.

The small dose of Magnesium Trisilicate controlled the acid effectively for somewhat over 30 minutes as compared with the control, and the subsequent rise in the acidity values was slightly less than in the control. The initial effect of milk was not so marked, but subsequent acid control was excellent.



Case No. 12.....

Name Miss F.....

Age 53..... Date 28th Dec. 1937.....

Diagnosis "Hyperchlorhydria".....

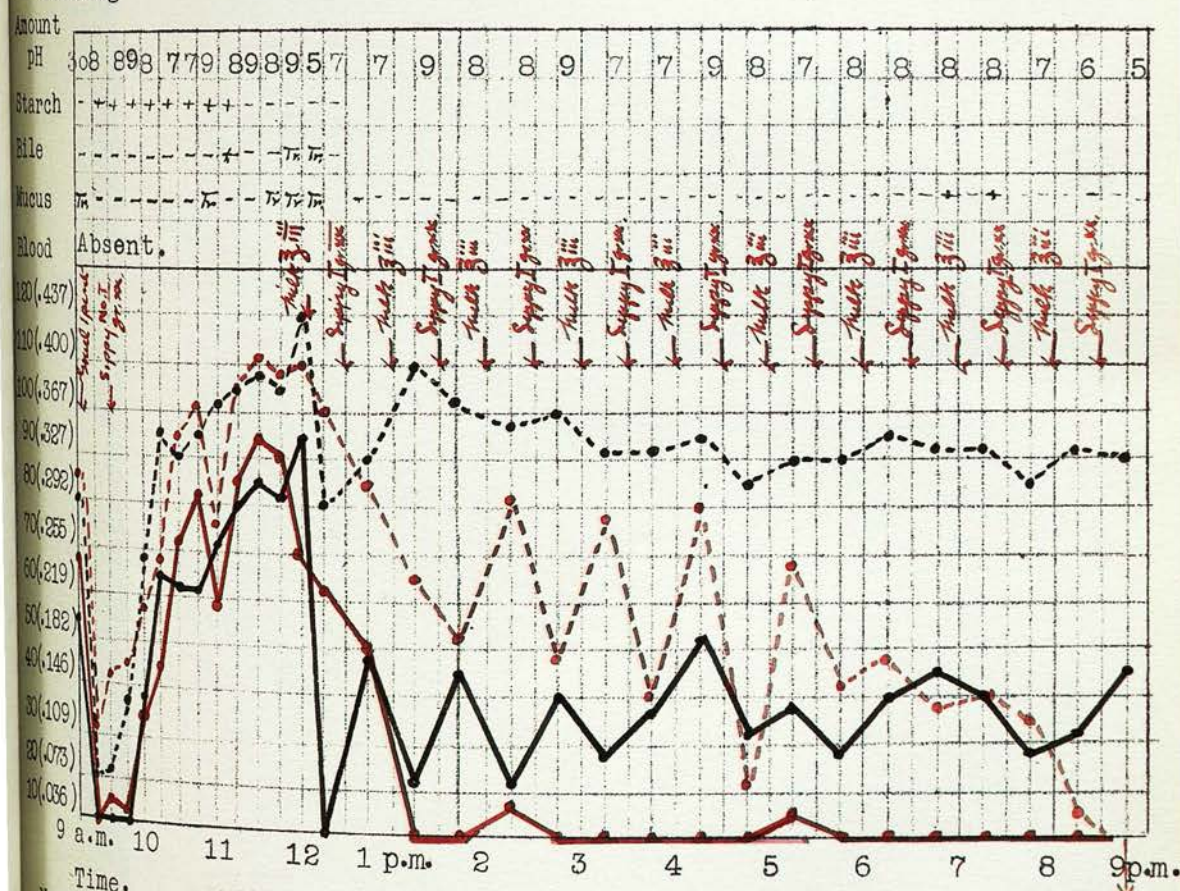
Substances given:- Milk - as indicated below. Gruel 1 pint.

A. "Food". Sippy Powder No. I. - as indicated.  
(Gr. xx. in water 1oz.)Pasting juice. Amount 30..... c.c.  
Special Characters - none.....  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Pasting



Notes:-

Control shown in black.

In this case the single dose of alkali had a very transient effect, (15 to 30 minutes), and this was followed by a rise in acid if anything greater than in the control.

After one hour milk and powders succeeded in reducing the acid again, and after this control was almost complete, but at the end of the day the gastric contents became slightly alkaline.

Emptying time would appear, from iodine test for starch, to have been accelerated by about one hour.

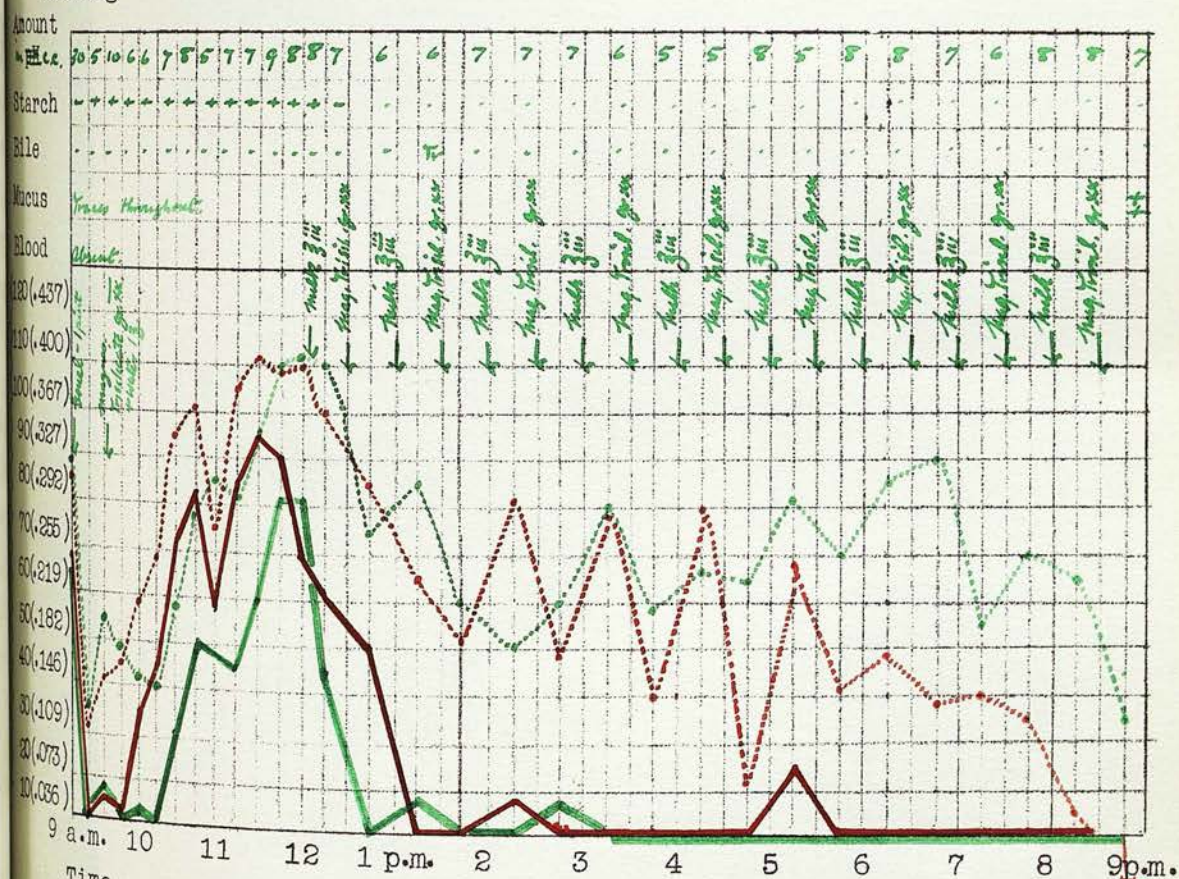


Case No. 12.....  
 Name Miss F......  
 Age 53..... Date 30<sup>th</sup> Dec. 1937.....  
 Diagnosis "HYPERCHLORHYDRIA.".....  
 Substances given:-  
 A. "Food". Milk 3 1/2 hourly from noon: Gruel - 1 pint at 9am.  
 B. Antacid(s). Magnesium Trisilicate gr.xx. at 9.30am.,  
12.30 pm, and hourly thereafter (in water 3i).  
 Fasting juice. Amount..... 30..... c.c.  
 Special Characters.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- Corresponding tests with Sippy Powder No. I. indicated in red.

In this case Magnesium Trisilicate gr.xx. controlled the "free" acidity response to the gruel test meal for 30 minutes longer than the same dose of Sippy Powder No. I. The subsequent acid secretion was less, and neutralisation of this acid was more quickly attained with milk and powder in the case of Magnesium Trisilicate.

While milk and powders were being given acid control was good in both cases. Magnesium Trisilicate would appear to be the better antacid however since the acid did not rise quite so high, whilst the reaction never fell below the neutral point as it did on one occasion with Sippy Powder No. I.

No acceleration of emptying time indicated.

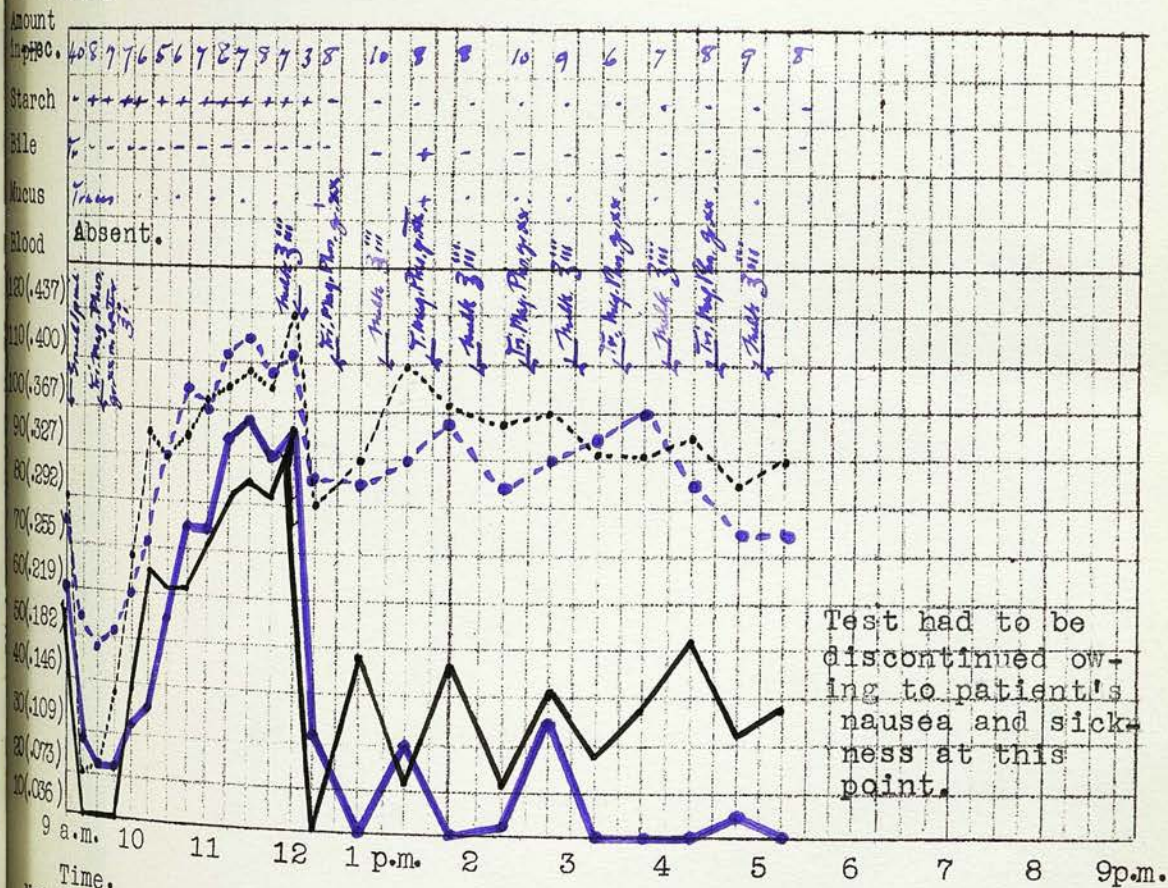


Case No. 12......  
 Name Miss F......  
 Age 53...... Date 1st. Jan. 1938......  
 Diagnosis "Hyperchlorhydria.".....  
 Substances given:- Gruel and milk - as indicated.  
 A. "Food". .....  
 B. Antacid(s). Tribasic Magnesium Phosphate - as indicated.  
 Pasting juice. Amount 40 (Gr.xx. in water 1oz.)  
 Special Characters.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- Control (in black) .

The two specimens withdrawn before the powder was given would seem to indicate that the acid response would have been higher on this day than on the day of the control, but, even so, the neutralising effect of this powder is very transient and incomplete, whilst the following stimulant effect exceeds that of the control or either of the other two powders tested.

Even when given hourly between milk feeds the result is not satisfactory, and, even with this incomplete test it is shown that, in this case at least, Tribasic Magnesium Phosphate is the least efficient of the antacids tested.

Emptying time did not appear to be notably affected.



## CASE NO. 13.

MR. D.D.

Aged 66.

Complaints. Alleged melaena on day of admission.

"Indigestion attacks" for 20 years with  
 story of epigastric pain after food  
 suggesting duodenal ulcer.

Examination. Clinically - nil to note.

Test meal - hyperchlorhydria .

Faeces - never occult blood.

Barium Series - no ulcer ,but a divert-  
 iculum of the duodenum .

Diagnosis. Hyperchlorhydria with diverticulum of duo-  
 denum ; auricular fibrillation.

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

I. Effects of antacids (gr. 20 .) on three hour test.

Magnesium Trisilicate , Sippy No. I. , and Tribasic Mag-  
 nesium Phosphate all reduced the acid for about 15-30  
 minutes this being followed by a very marked second-  
 ary secretion far exceeding the control, highest with  
 Sippy Powder and most prolonged with the other two.

The control showed a marked hyperchlorhydria.

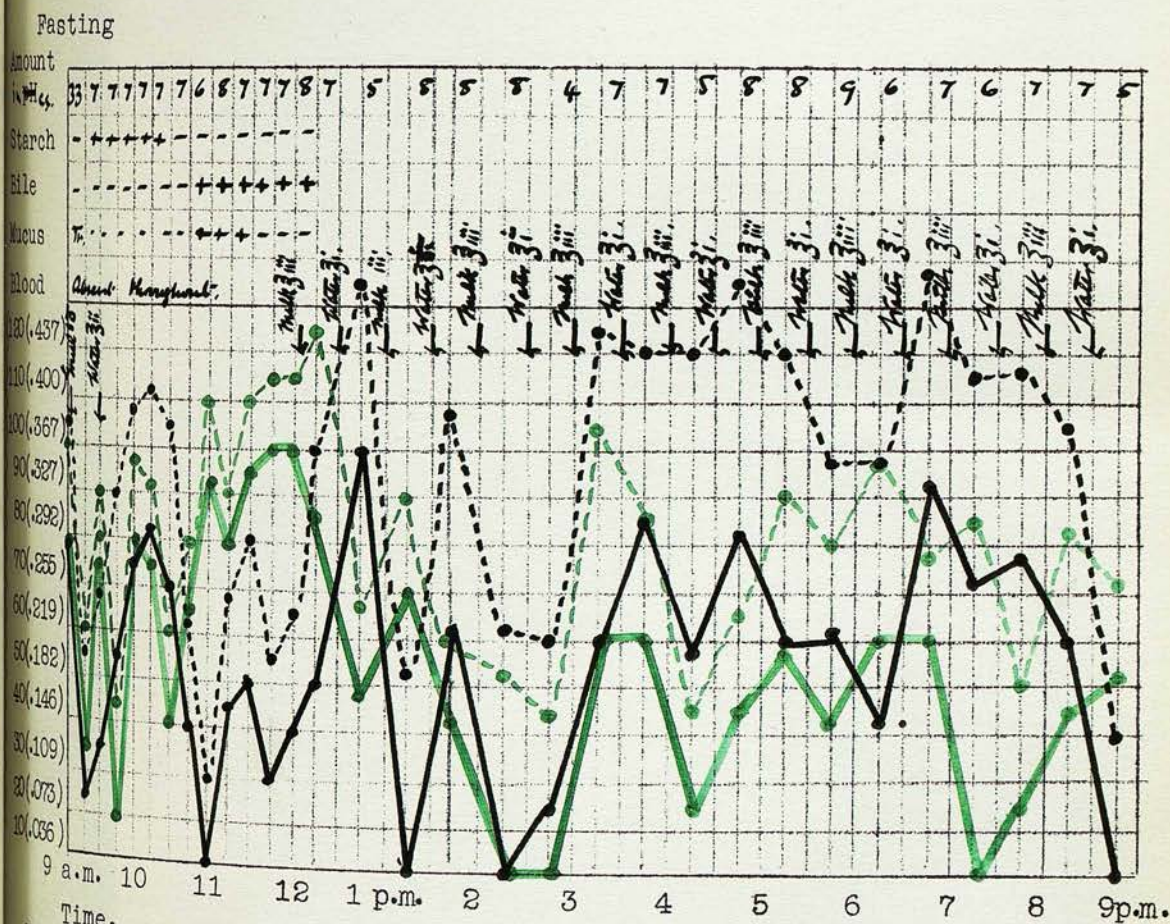
II. Effects of antacids on nine hour test.

After 3oz. hourly milk feeds a high acidity was  
 almost constantly present and this was only slightly  
 modified by the hourly antacids. Magnesium Trisilicate  
 was the least unsatisfactory and Sippy No. I. the most,  
 since, when the latter did control the acidity the  
 action was excessive an alkaline reaction being  
 produced in the stomach.



Case No. ....13.....  
 Name.....Mr. D.D.....  
 Age.....66..... Date.....30<sup>th</sup> Dec. 1937.....  
 Diagnosis.....*Hypochlorhydric, with chylomicronemia of cholesterolemia.*  
 Substances given:-  
 A. "Food". ..*Equal amtl. milk - as indicated +*  
 B. Antacid(*o*). *Water: as shown for control test.*  
 Fasting juice. Amount.....33..... c.c.  
 Special Characters.....*none*.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.  
 ..... represents total acidity.



A case of hyperacidity showing the complete inadequacy of the small milk feeds for the control of the acidity they stimulate.

The 20 gr. dose of Magnesium Trisilicate reduced the acid level for little more than 15 minutes after which it rose to and remained at a higher level than that prevailing in the control. In the rest of the test this powder achieved little more than the milk feeds alone.

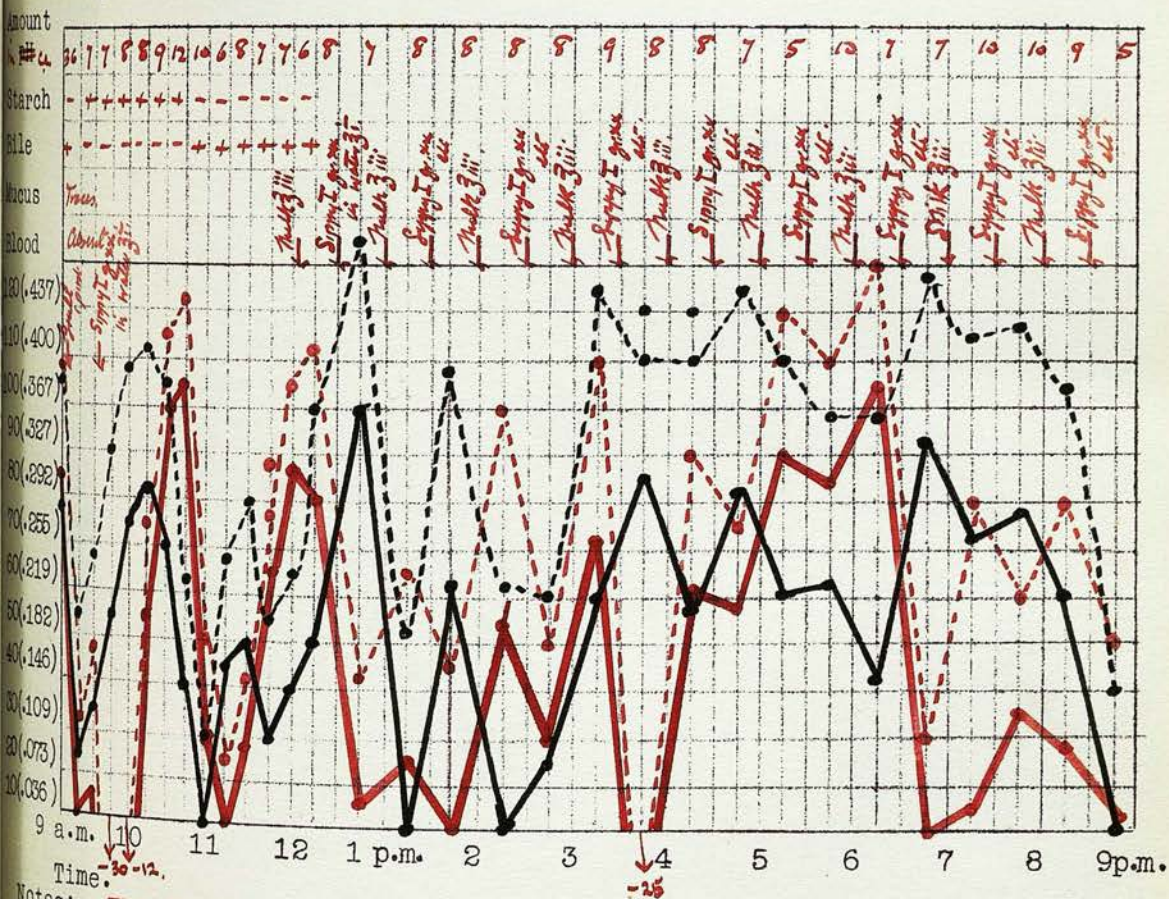


Case No. 13.....  
 Name..... Mr. D. D......  
 Age..... 66..... Date..... 1<sup>st</sup> Jan. 1938.....  
 Diagnosis..... Hypochlorhydria with cholecystitis of cholelithiasis.....  
 Substances given:-  
 A. "Food". Gruel and milk feeds - as indicated.  
 B. Antacid(s). Sippy Powder NO. 2 - gr. xx - as indicated  
in water 3i.  
 Fasting juice. Amount..... 36..... c.c.  
 Special Characters..... none.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

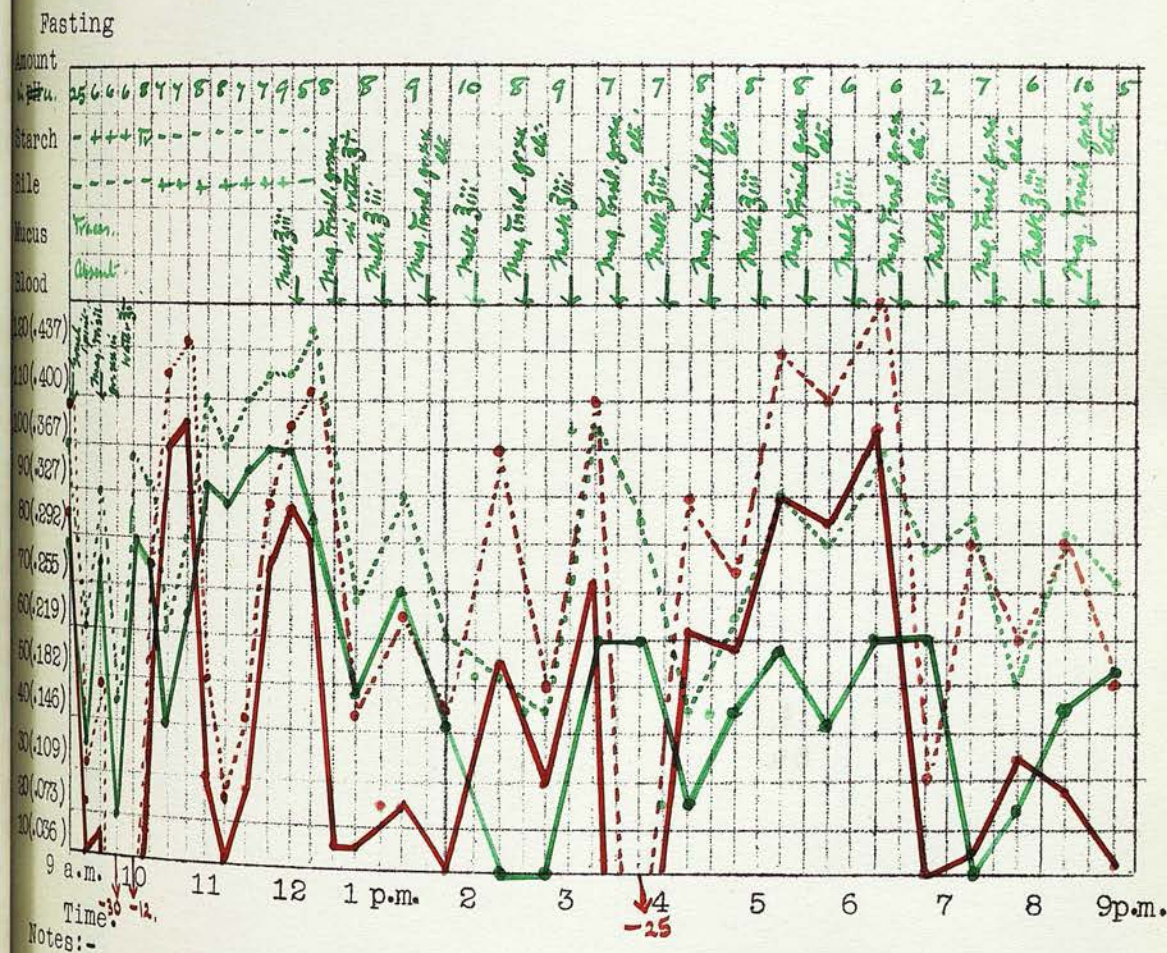
Fasting





Case No. 13.....  
 Name Mr. D. D......  
 Age 66..... Date 3<sup>rd</sup> Jan. 1938.....  
 Diagnosis Hypochlorhydria with duodenal & duodenal.....  
 Substances given:-  
 A. "Food" Gruel and Magnesium Trisilicate + with hourly.....  
 B. Antacid(s). Milk feeds of 3oz. - as indicated.....  
 Fasting juice. Amount 25..... c.c.  
 Special Characters none.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.  
 ..... represents total acidity.



This chart shows the completely inadequate control of acidity which may exist even with a strict and intensive regime.

Magnesium Trisilicate's effect was on the whole more satisfactory than that of the Sippy Powder in controlling the acid while it did not at any time produce an alkaline reaction in the stomach; it could, too, be given in much larger doses without the danger of alkalosis which would certainly arise with Sippy No. I.

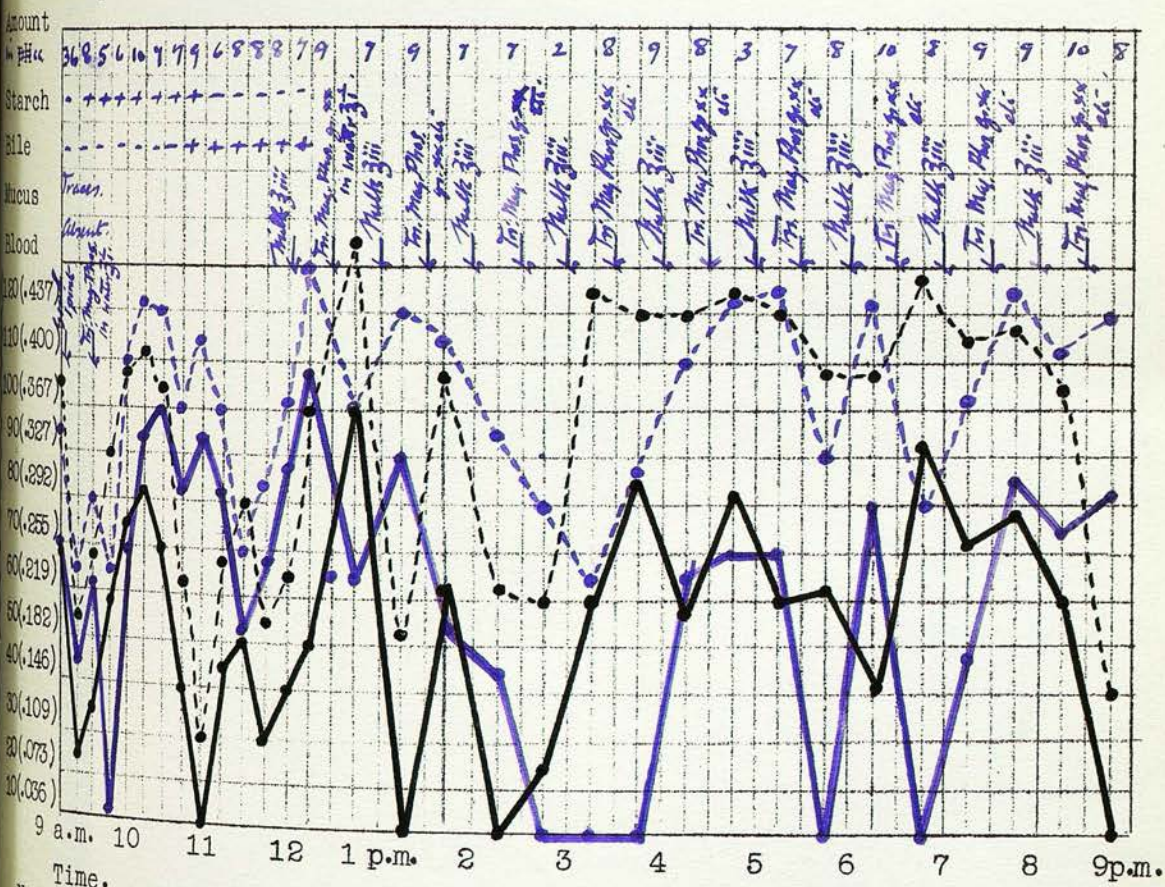


Case No. 13.  
Name Mr. D. D.  
Age 66 Date 5<sup>th</sup> Jan. 1938.  
Diagnosis. Hypertension with diverticulum of the duodenum.  
Substances given:-  
A. "Food". Gruel and milk feeds (3oz) - as indicated.  
B. Antacid(s). Trisbasic Magnesium Phosphate, - as indicated.  
Fasting juice. Amount 36. c.c.  
Special Characters none.  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

## Fasting



Notes:- 15 minutes acid reduction followed by marked and prolonged secondary stimulation resulted from the 20 gr. dose Tribasic Magnesium Phosphate.

In the remainder of the test the powders achieved little controlling the "free" acidity.



In the remainder of the cases (i.e. eleven)  
aluminium hydroxide has been substituted for tribasic  
magnesium phosphate, and in the initial single dose  
test the amount has been increased for all antacids  
from twenty grains to one drachm.

In the next three cases the second part of the  
test remains as before, with aluminium hydroxide in  
place of tribasic magnesium phosphate.

---

CASE NO. 14.

MR. M. A.

Aged - 60.

Complaint. Epigastric pain one hour after food  
going away before the next meal---6 months.

Examination. Clinically - negative.

Test meal - hyperacidity.

Faeces - no occult blood.

Barium series - "no ulcer seen  
Duodenal ileus".

Diagnosis. Peptic ulcer and duodenal ileus.

#### SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

##### I. Effect of one drachm of antacids on three hour test meal result.

Magnesium Trisilicate reduced the acid for  $1\frac{1}{2}$  hours  
Aluminium Hydroxide had a similar but less complete  
effect for about the same time while Sippy No. I had  
almost no antacid effect in this case. None produced  
a real stimulant action and Aluminium Hydroxide  
appeared to depress the acidity throughout the test.

##### II. Effect of the antacids on nine hour test in hourly 20 gr. doses.

The milk feeds controlled the acid well except for  
one period. Aluminium Hydroxide exerted an excellent  
effect, but Sippy No. I. caused the stomach contents  
to become alkaline very frequently and did not com-  
pletely control the acid. Magnesium Trisilicate had  
an action intermediate.

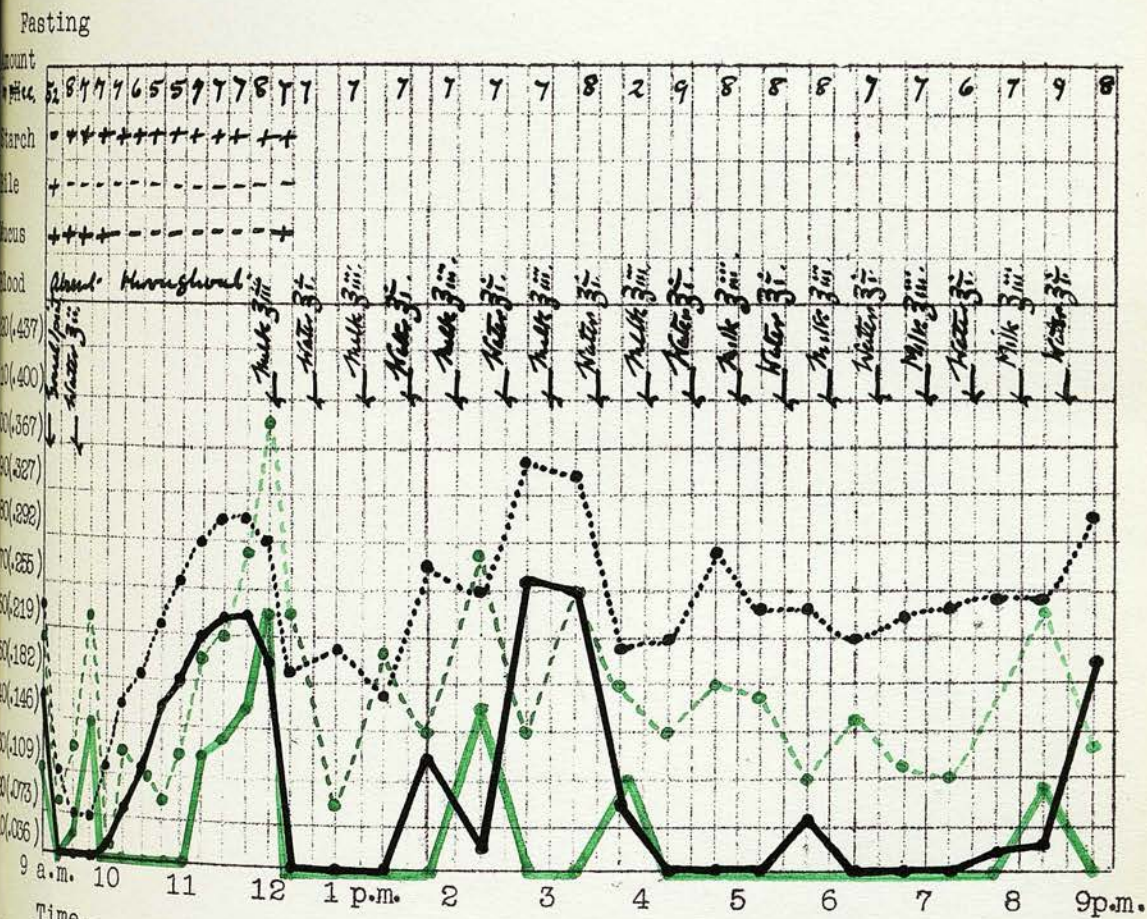


# ANALYSIS OF GASTRIC CONTENTS. CONTROL.

144.

Case No. 14.....  
 MR. M. A. ....  
 Date 15th Jan. 1933.....  
 Diagnosis Peptic ulcer and duodenal ileus.....  
 Substances given:-  
 A. "Food". Gruel and milk feeds.....  
 B. Antacid(s). None but milk feeds.....  
 Fasting juice. Amount 52..... c.c.  
 Special Characters none.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.  
 ..... represents total acidity.



Notes:-  
 Antacid effect of about 1½ hours following Magnesium Trisilicate with fairly good control subsequently.  
 The test shows that milk alone except for one hour was fairly successful in dealing with the acid.



SIPPY NO. I. TEST.Case No. 14.....

MR M .A. ....

Date 21ST. JAN. 1938.....Diagnosis PEPTIC ULCER AND DUODENAL ILEUS......Substances given:- GRUEL AND MILK FEEDS--30Z......

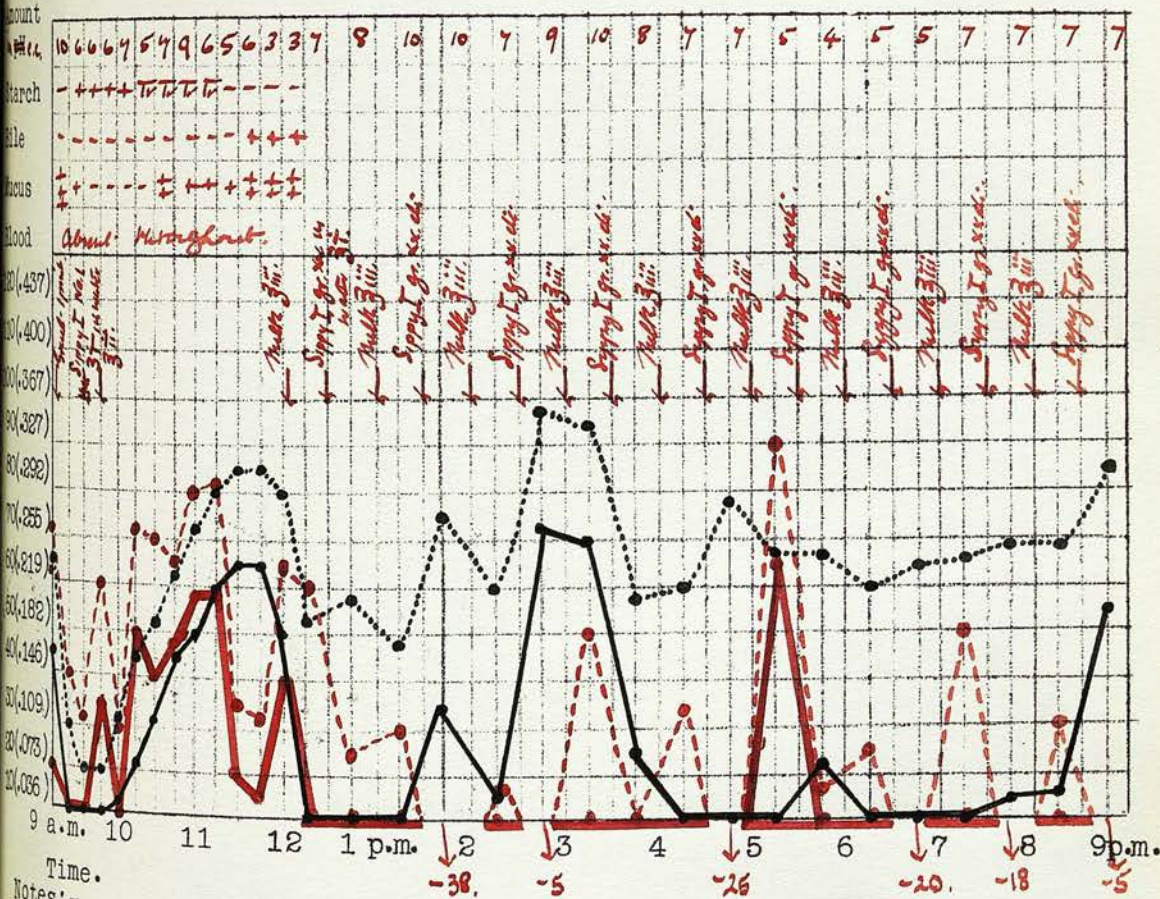
A. "Food".....

B. Antacid(s) SIPPY NO. I. 1/2 S. INDICATED.....Fasting juice. Amount 10..... c.c.  
Special Characters NONE.....  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



This shows the transient action of even the large dose of Sippy No. I. with rapid rise of acid to the control level.

The action in the remainder of the test was most unsatisfactory since the stomach contents were so often alkaline while on one occasion the acidity rose to 55 points.

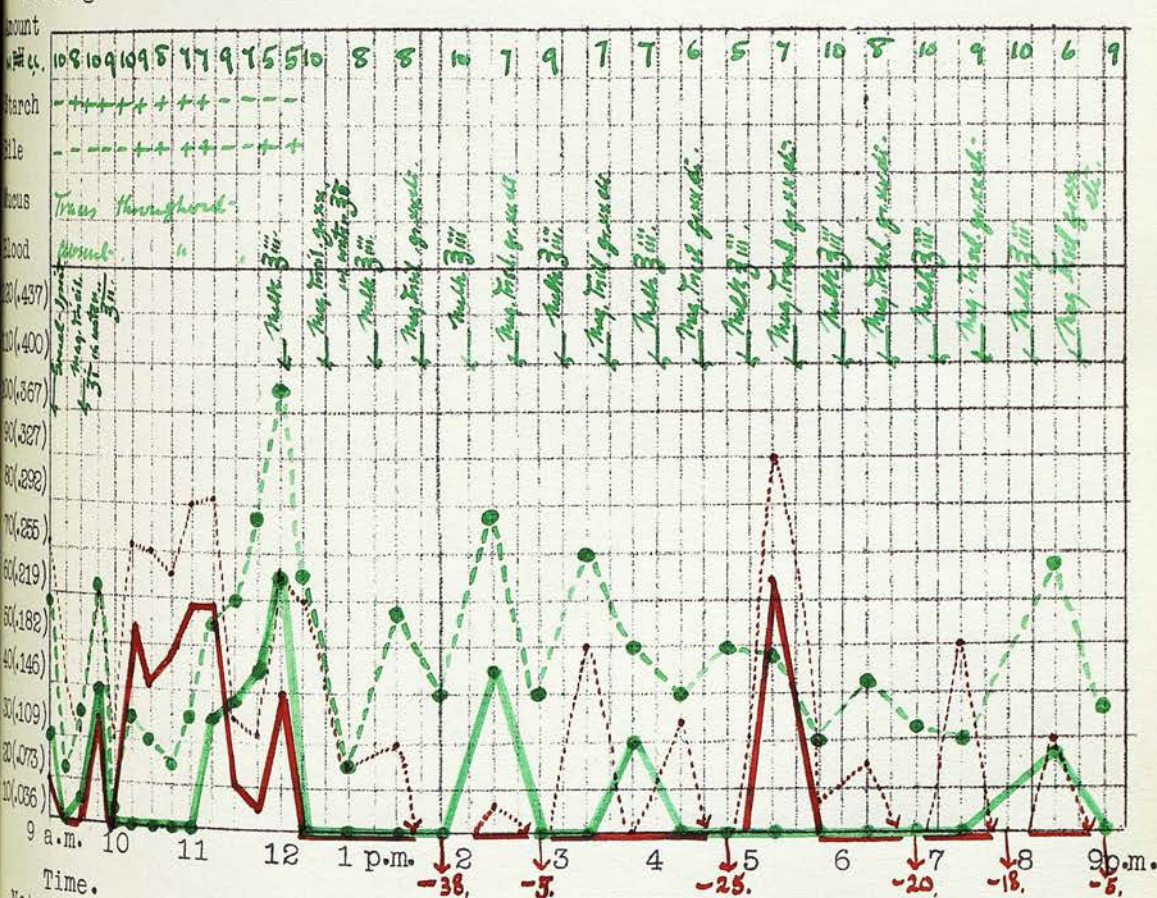


Magnesium Trisilicate Test.Case No. 14.....Name Mr. M. A......Age 60..... Date 19th January, 1938.....Diagnosis Peptic Ulcer and Duodenal Ulcer.....Substances given:- Gruel and milk feeds - as indicatedA. "Food".....  
B. Antacid(s) Magnesium trisilicate gr. xx and 3T - as indicatedFasting juice. Amount..... 10..... c.c.  
Special Characters..... none.....  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



This illustrates well the advantages of the neutral antacid over Sippy No. I. with its powerful alkaline properties. A slightly larger dose of the former would probably have completely controlled the acid with no danger of alkalosis.







## CASE NO. 15.

MR. G. McG.

Aged - 31.

Complaint - Epigastric pain one hour after food going away before the next meal--- ----2 years.

Examination - Clinically - negative.

Test meal - Hyperacidity.

No occult blood in faeces.

Barium series - "duodenal ulcer".

Diagnosis . Duodenal ulcer.

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

I. Effect of one drachm of antacids on three hour test meal.

Sippy no. I. and Magnesium Trisilicate each controlled the acid for  $2\frac{1}{4}$  hours and Aluminium Hydroxide for  $1\frac{3}{4}$  hours. None was followed by a stimulant action and the first was the best in this case.

II. Effect of 20 gr. of antacids hourly on nine hour test with hourly three ounce milk feeds.

Milk alone was quite unable to control the acidity but this was much improved by all three antacids of which Aluminium Hydroxide was the best.

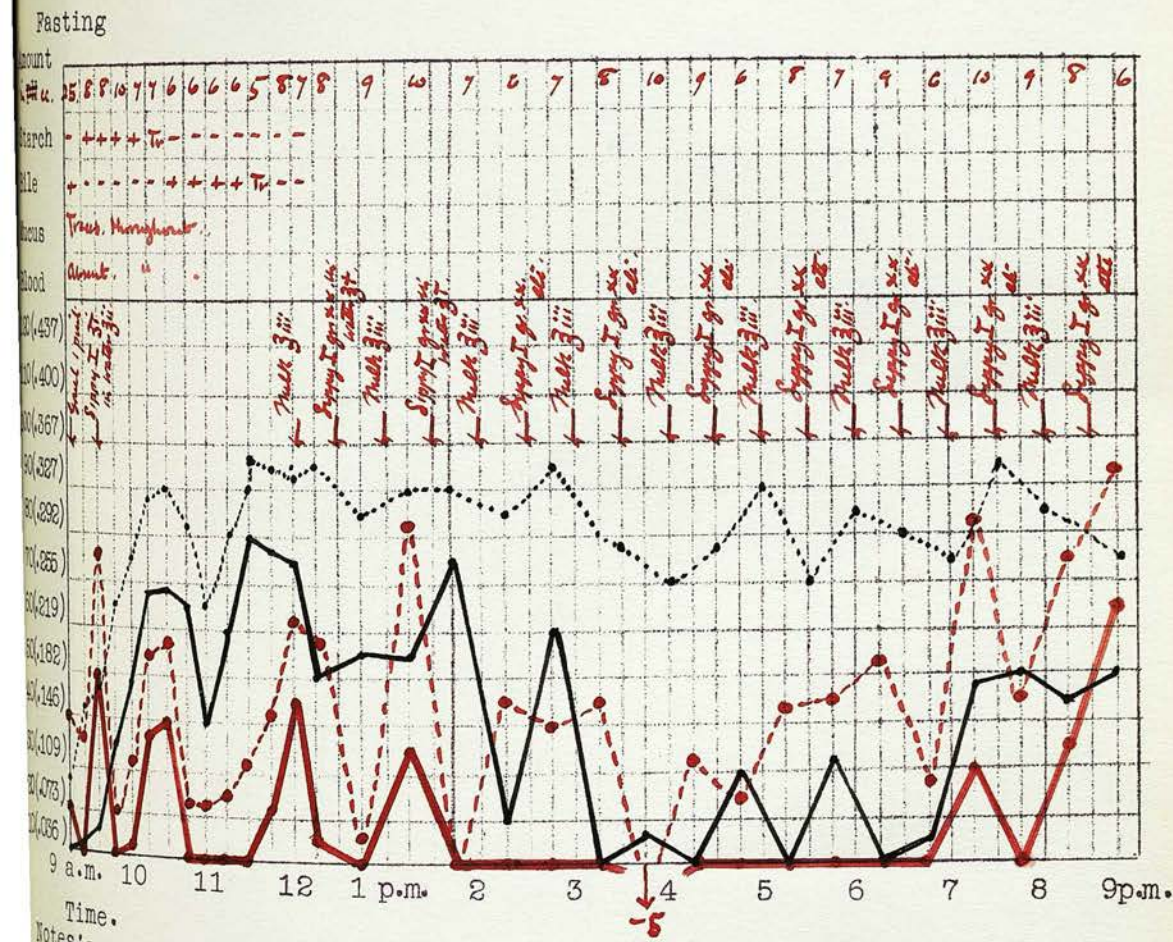




Case No. 15.....  
 Name..... *Mr. J. S. M. G.*.....  
 Age..... 31.....  
 Date..... *23<sup>rd</sup> Jan. 1938.*.....  
 Diagnosis..... *Diverticular Ulcer.*.....

Substances given:- *Gruel 1 pint: Milk feeds 3/4 hourly: as indicated.*  
 A. "Food".....  
 B. Antacid(s) *Sippy Powders No. I. - 3T after gruel and*  
*gn. xx hourly between milk feeds: as indicated.*  
 Fasting juice. Amount..... *25 cc.*..... c.c.  
 Special Characters.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.  
 ..... represents total acidity.



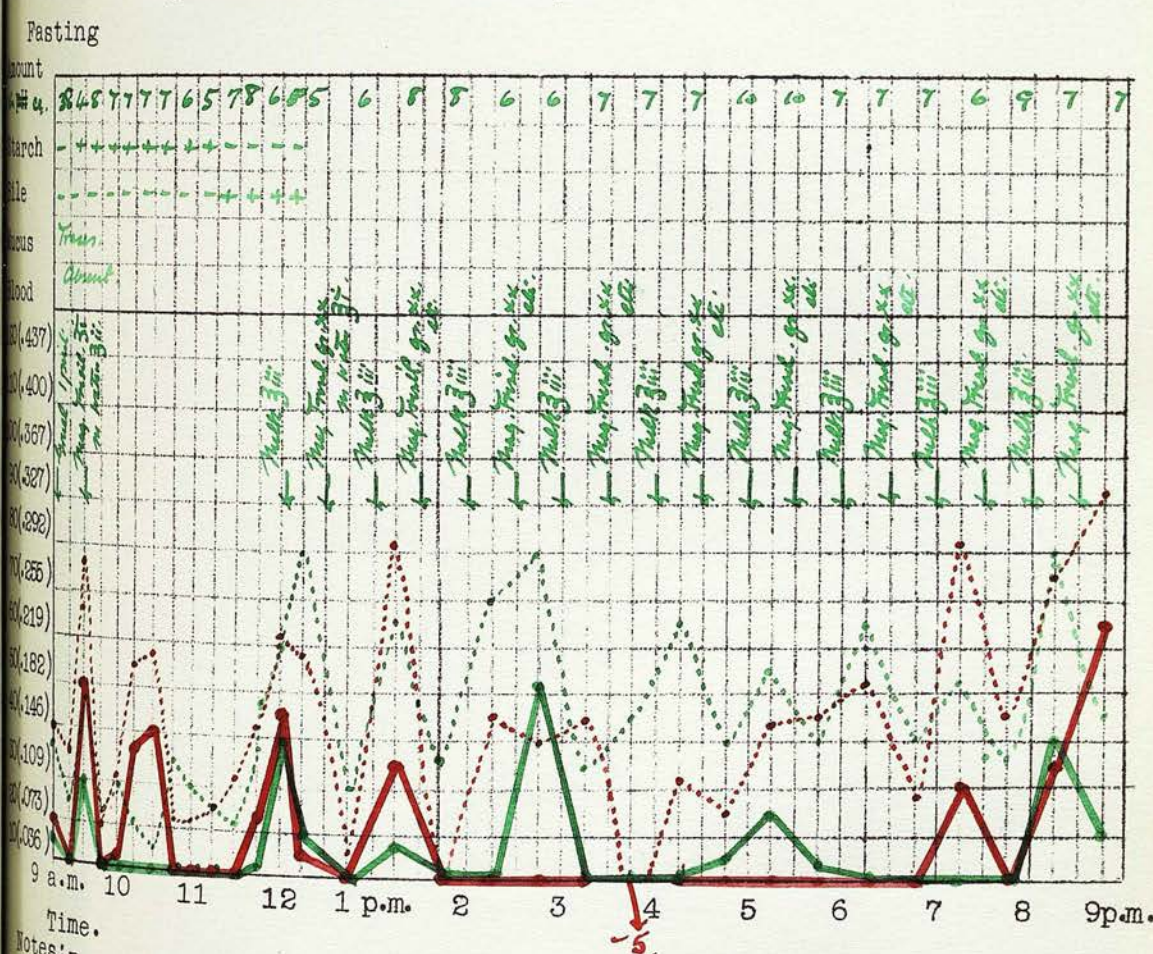
Some degree of effect on acidity can be observed for 4 hours after initial dose and no stimulant effect seen. (Acidity rise at 10.15 a.m. probably due to lack of diffusion of powder through the stomach contents.)

Control in the remainder of the test good except in the last hour.



Amount.....<sup>38</sup> c.c.  
Special Characters.....  
Acidity, etc. (See first column below.

..... represents free HCl.  
..... represents total acidity.



Magnesium Trisilicate appears if anything the better antacid in this test. Note that while not completely controlling the acid in the nine hour test Sippy No.I. at one point caused the stomach contents to become alkaline.

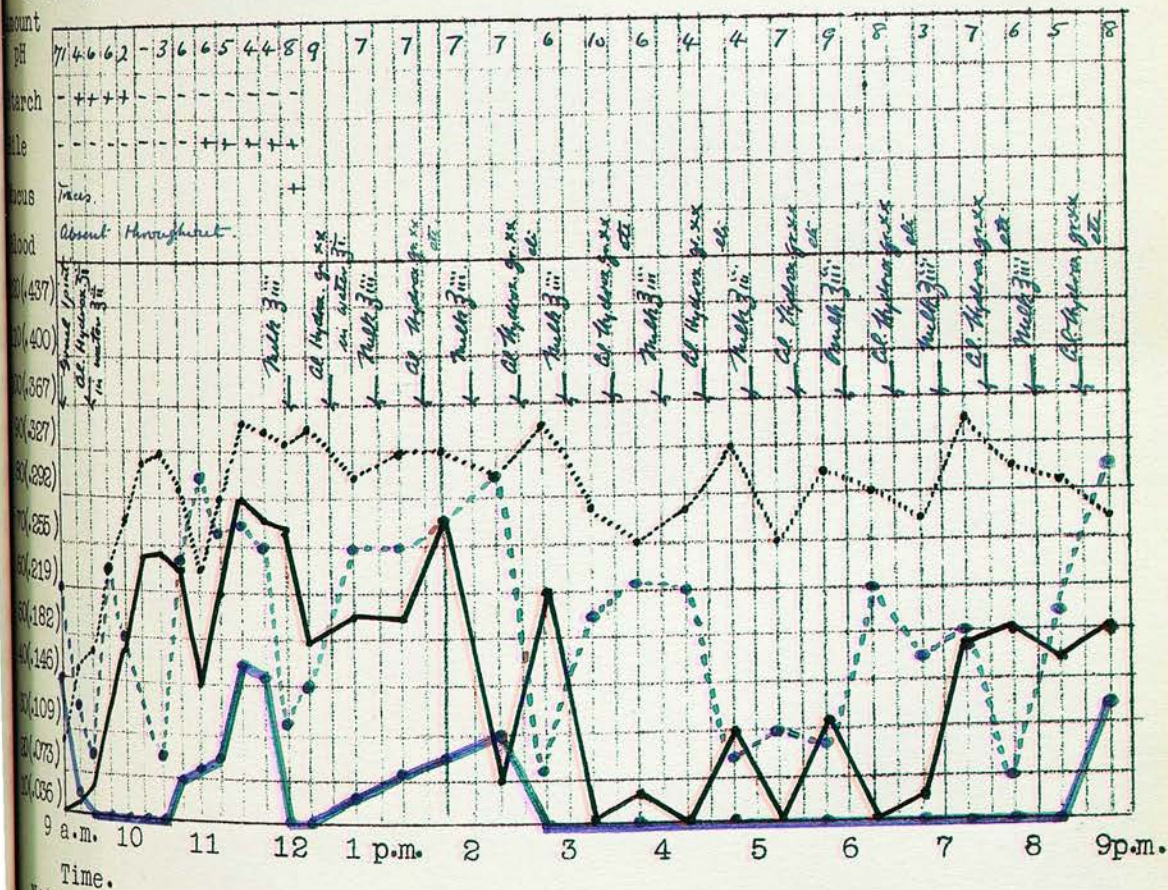


Case No. 15.....  
 Name Mr. S. M. G......  
 Date 27<sup>th</sup> Jan. 1938.....  
 Age 31.....  
 Diagnosis Duodenal Ulcer.....  
 Substances given:-  
 A. "Food". Equal. cond. milk feeds - as indicated......  
 B. Antacid(s). Aluminium Hydroxide - as indicated......  
 Fasting juice. Amount 71..... c.c.  
 Special Characters.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:-

12 hours antacid effect of initial dose of one drachm Aluminium Hydroxide with no stimulant action.

Note that the best control in the second part of the test was obtained with this antacid.



## CASE NO. 16.

MRS. E.S.

AGED : 61.

COMPLAINTS : Epigastric pain and vomiting - 3 days.

"Bilious attacks" with same pain- 40 years.

EXAMINATION: Obese patient with tenderness in the  
right hypochondrium on admission.

Cholecystography - "Poorly functioning gall bladder"

Barium Series - Not done.

Test Meal - Hyperchlorhydria.

DIAGNOSIS: Chronic cholecystitis and hyperchlorhydria.

SUMMARY OF GASTRIC CONTENTS' ANALYSES.I. EFFECT OF ANTACIDS ON ACID RESPONSE TO THREE  
HOUR GRUEL TEST MEAL.

The control showed low fasting acidity followed by high response to gruel. This was adequately controlled for just over two hours by 1 drachm of Magnesium Trisilicate given 30 minutes after the meal. Sippy Powder No. I. and Aluminium Hydroxide both resulted in control of about  $1\frac{1}{2}$  hours; the former, however, caused an excessively alkaline reaction to be produced; the latter caused the smallest subsequent rise in acidity, which in the other two was only moderate not at any time attaining the high level of the control.

## II. EFFECT OF ANTACIDS ON ACIDITY RESPONSE TO 30Z.

## MILK FEEDS HOURLY - 9 HOUR TEST.

All three of the above powders completely neutralised the high "free" acidity throughout the entire period.

NOTE THE INADEQUACY OF MILK AS AN ANTACID HERE.







Case No. 16. SIPPY NO. I. TEST. (CONTROL IN BLACK).

MRS. E.S.

61.

Date. 7th. Jan. 1938.

Diagnosis. CHRONIC. CHOLECYSTITIS. AND. HYPERCHLORHYDRIA.

Substances given:- GRUEL AND MILK FEEDS - AS INDICATED.

A. "Food". SIPPY NO. I. - " " " "

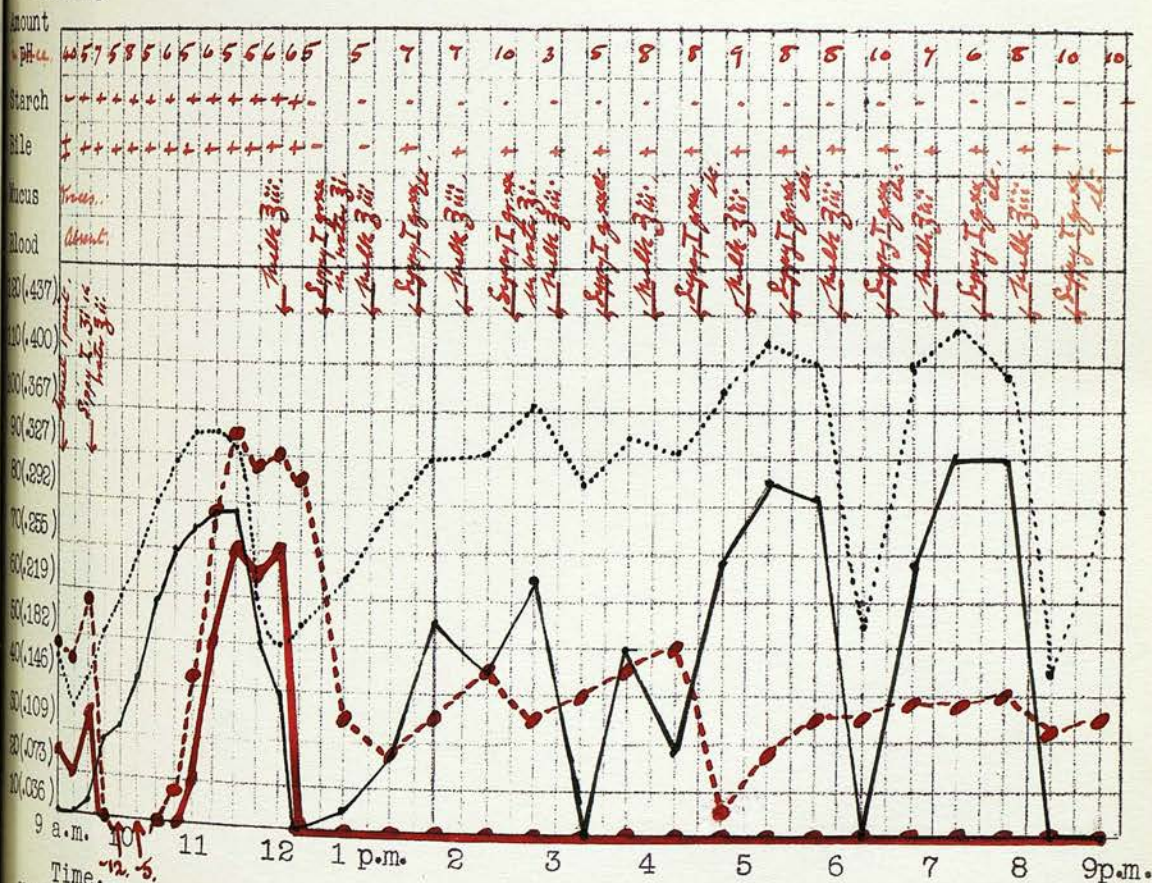
B. Antacid(s). " " " "

Fasting juice. Amount. 40. C.C.  
Special Characters. NONE.  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- Sippy No. I. drachm I., produced an excessive antacid effect, but kept the gastric acidity at a low level for almost two hours. This was not followed by as great an acid secretion as might have been expected from the results in other tests.

Complete "free" acid neutralisation was achieved in the second part of the test without excessive effect.

No noteworthy alteration in emptying time occurred.



# ANALYSIS OF GASTRIC CONTENTS.

156.

MAGNESIUM TRISILICATE TEST. (SIPPY NO. I. IN RED).

MRS. E. S.

61.

Date... 5th. Jan. 1938.

CHRONIC CHOLECYSTITIS WITH HYPERCHLORHYDRIA.

Substances given:-

GRUEL AND MILK FEEDS AS INDICATED.

A. "Food". ... MAGNESIUM TRISILICATE AS SHOWN:..

B. Antacid(s). .....

Pasting juice.

Amount..... 30..... c.c.

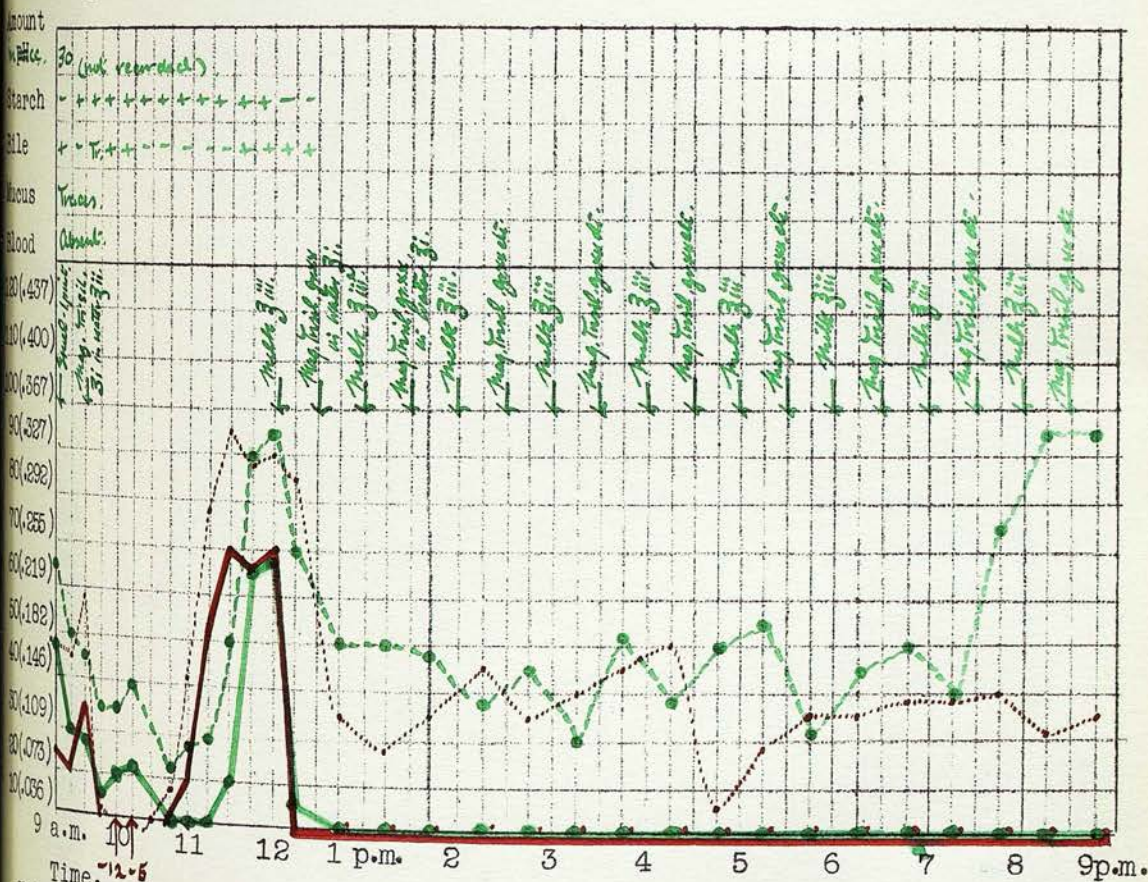
Special Characters..... NONE.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Pasting



Notes:- This chart shows the more "physiological" and prolonged effect of a single large dose of Magnesium Trisilicate as compared with Sippy Powder NO. I. There is considerable acid concentration and secretion immediately following this effect, but in neither is the control level exceeded.

In the second part of the test both powders produced an excellent result.

Emptying time apparently unaffected.



Case No. 16. ALUMINIUM HYDROXIDE TEST. (CONTROL IN BLACK).

MRS. E.S.

Date. 10TH. JAN. 1938.

Diagnosis. CHRONIC CHOLECYSTITIS WITH HYPERCHLORHYDRIA.

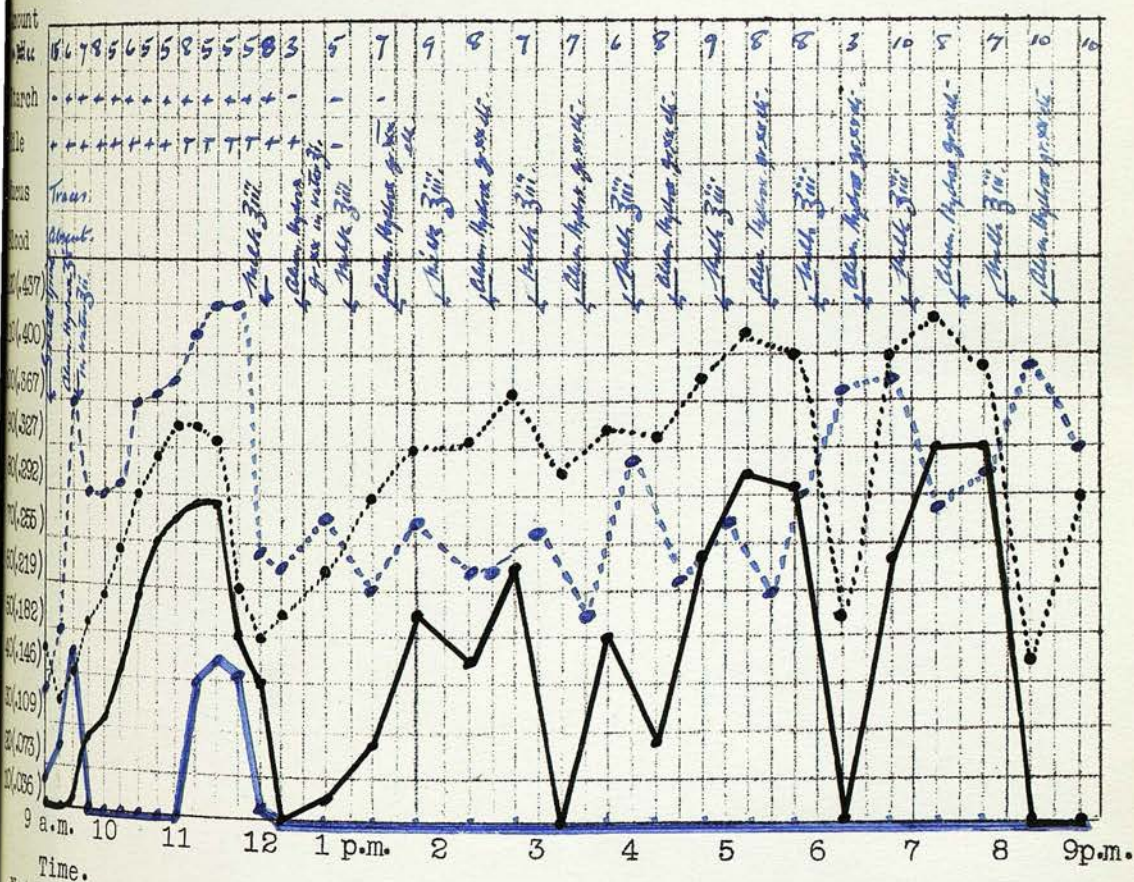
Dietary instructions given:- GRUEL AND MILK FEEDS AS INDICATED.  
A. "Food". ALUMINIUM HYDROXIDE AS INDICATED.  
B. Antacid(s).

Antacid juice. Amount. 15. c.c.  
Special Characters. NONE.  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Throughout the remainder of the test "free" acid neutralisation was complete.

Motility apparently unaffected.

In the next eight cases Sippy Powder No.2 has been substituted for Sippy Powder No.1, and in the second part of the test the doses have been increased from twenty to forty grains hourly.

---



CASE NO. 17.

MR. J. R.

Aged - 38.

Complaint. Vomiting blood on day of admission.

Epigastric pain  $\frac{1}{2}$  hour after food and relieved by food -----7 years.

Examination. Clinically - Slight tenderness in epigastrium with hyperaesthesia.

Test meal - normal.

Faeces - occult blood present.

Barium series - not yet done.

Diagnosis. Haematemesis with peptic ulcer.

#### SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

##### I. Effect of antacid on three hour test meal result.

Magnesium Trisilicate and Sippy No 2, had each about 45 minutes antacid effect followed by some stimulant effect most marked with the former. (Higher acid values before powder given on this day however.) Aluminium Hydroxide's effect lasted rather more than two hours and was not followed by any stimulant effect.

##### II. Effect of antacids on nine hour test with milk feeds of three ounces hourly.

There was no great amount of acid left even on the control day but the powders did not succeed in completely controlling this in any case.

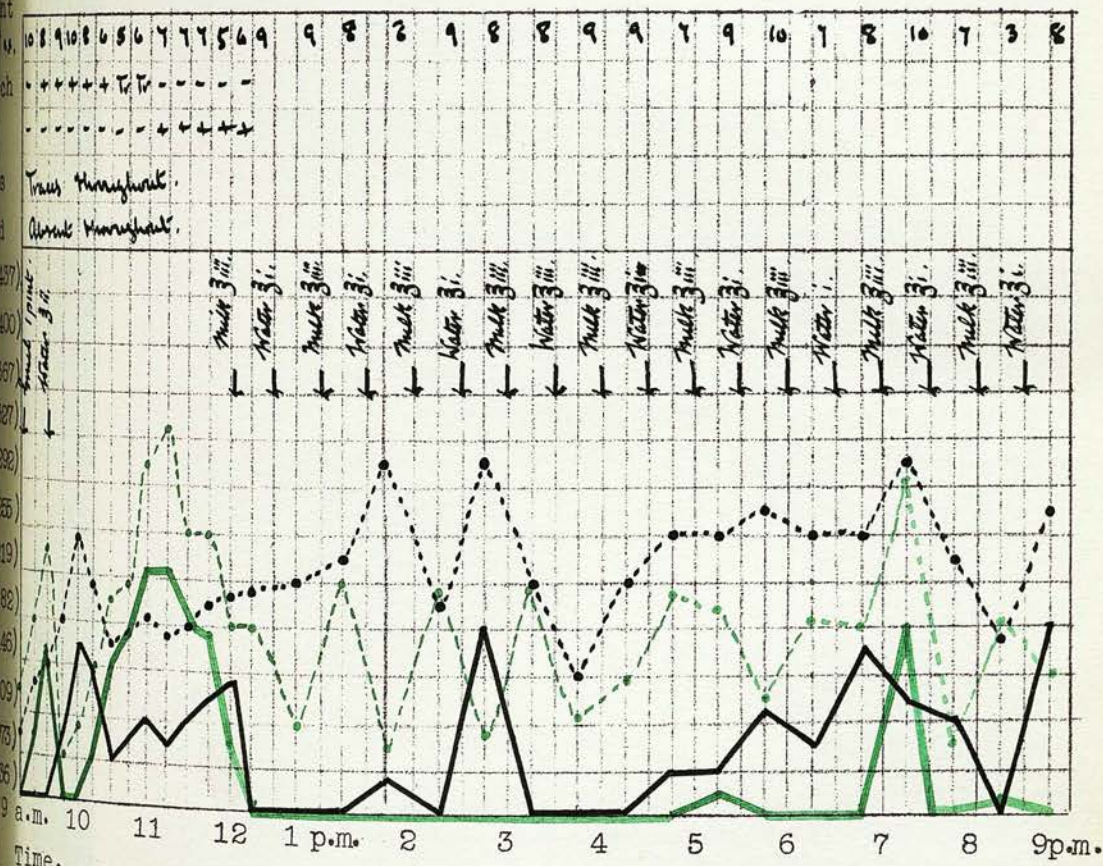
# ANALYSIS OF GASTRIC CONTENTS. MILK CONTROL TEST.

160.

No. 17:.....  
MR. J. R. ....  
Date... 7th March 1938.....  
Haematemesis; peptic ulcer.....  
Diet given:- Gruel and milk feeds - as indicated.  
A. "Food". ..... none but milk feeds.....  
B. Antacid(s). ..... none but milk feeds.....  
Amount... 10..... c.c.  
Special Characters..... none.....  
Acidity, etc. (See first column below.)

..... represents free HCl.  
..... represents total acidity.

Fasting



Notes:- A case of normal acidity which was affected for 45 minutes by 1 drachm of Magnesium Trisilicate, this being followed by secondary acid stimulation. (Note that the initial acidity values were higher on the day on which this antacid was given than on any of the other three days of the test.)  
Milk feeds controlled the acid fairly well without the aid of the powder which produced a result only a little better.



## ANALYSIS OF GASTRIC CONTENTS.

161.

SIPPY NO. II TEST.

Case No. 17.

MR. J. R.

Name.

Date 9th March 1938.

Age 38.

Diagnosis.

Haematemesis : peptic ulcer.

Substances given:-

A. "Food". Gruel and 3 oz. milk feeds- as indicated.

B. Antacid(s). Sippy No. 2. --initial dose 1 drachm.

--hourly doses grains 40.

Fasting juice.

Amount. 2 c.c.

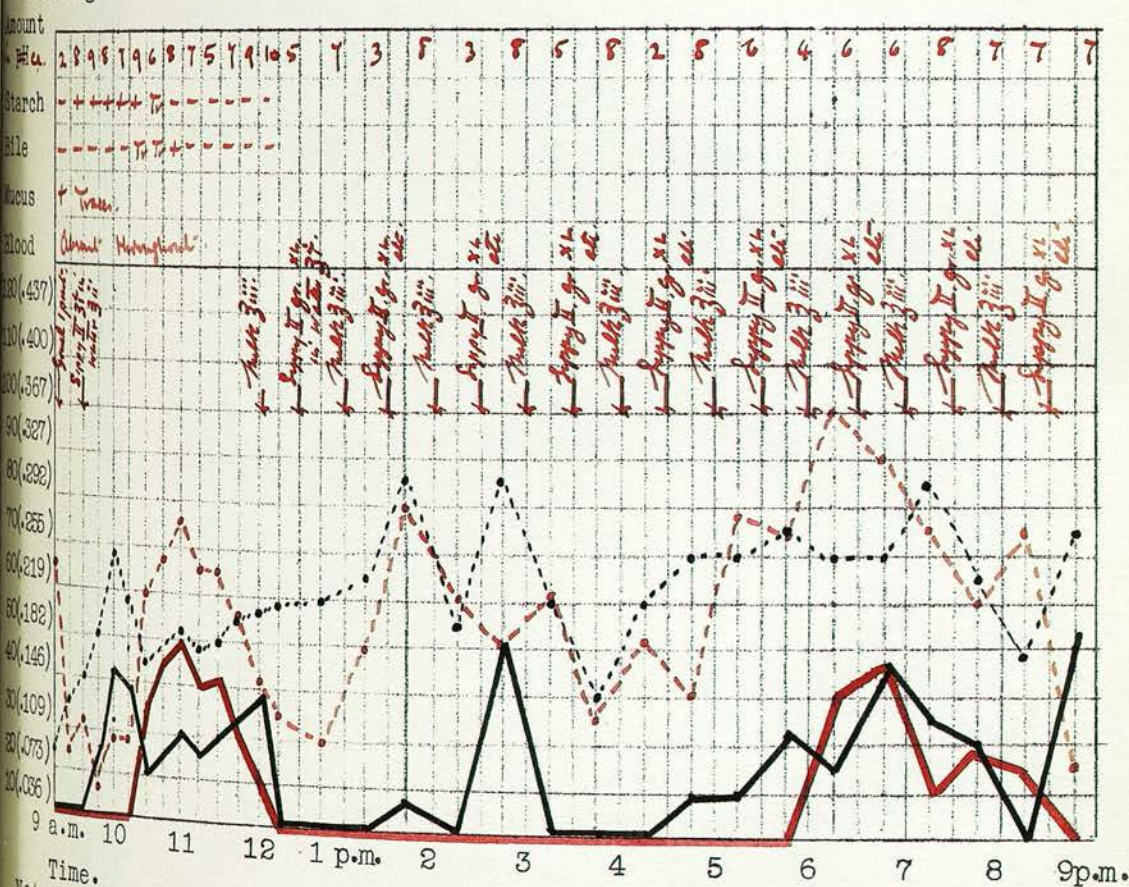
Special Characters. none.

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- 45 to 60 minutes antacid effect followed by slight stimulant effect. Subsequent control little better with Sippy No. 2. than with milk feeds alone.



Magnesium Trisilicate Test.

Case No. 17.....

Mr. J.R. ....

Date 11th March, 1938.

Diagnosis Haematemesis : peptic ulcer.

Substances given:-

A. "Food". Gruel and milk feeds 3oz - as shown.

B. Antacid(s) Magnesium Trisilicate - initial single dose - 1 drachm.  
- hourly later doses - gr. 40.

Fasting juice. Amount 18 c.c.

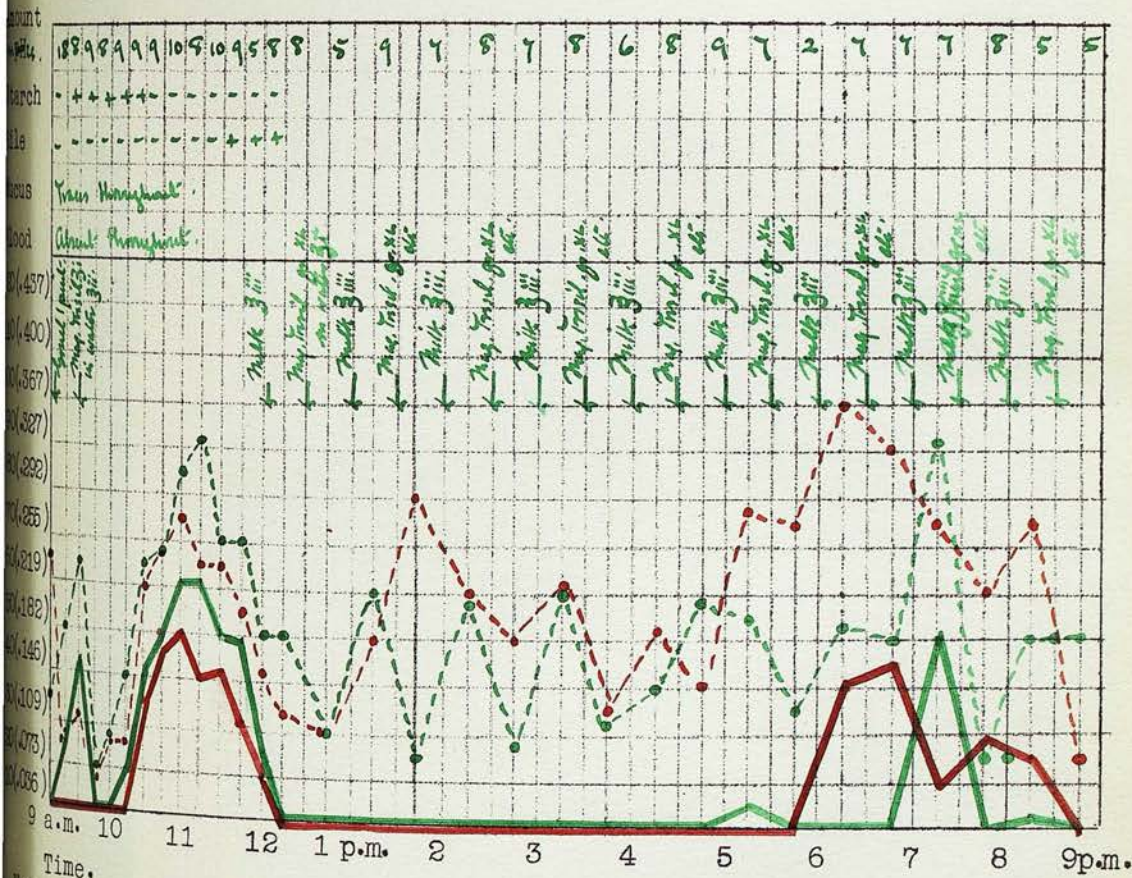
Special Characters none

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- The difference in the initial readings before the powders were given should be considered in assessing the effects of the two remedies. It would then appear that they have about the same effect in this case, and that a poor one both in the first and second parts of the test.



### Aluminium Hydroxide Test.

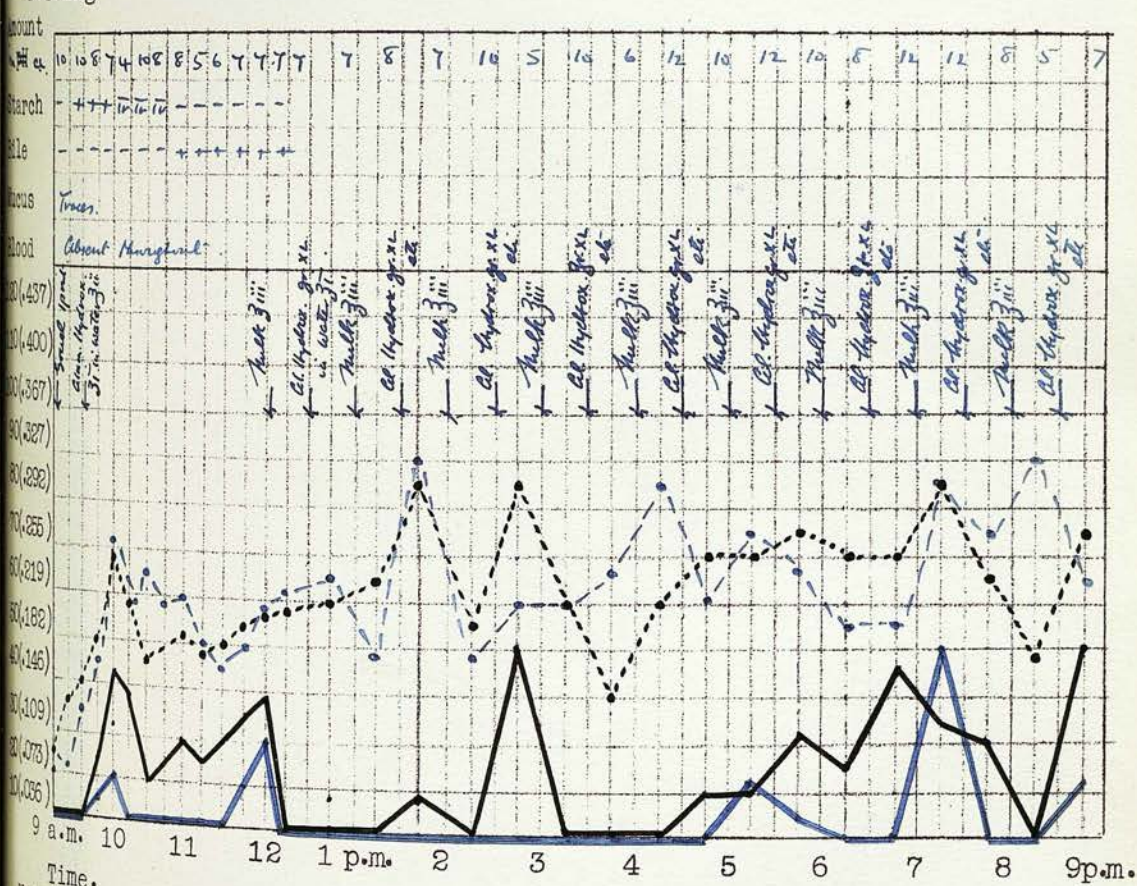
Case No. 17..... Aluminum Hydroxide Test.  
Name..... Mr. J. R.  
Age 38..... Date 13<sup>th</sup> March, 1938.  
Diagnosis..... Hematuria..... pyeloc. ulcer.

Substances given:- *Hyru* and 3oz. milk feeds - as indicated.  
A. "Food".  
B. Antacid(s). *Aluminum Hydroxide* - initial single dose - 1 drachm.  
- hourly doses. - 20 grains.  
Fasting juice. Amount..... *10*..... c.c.  
Special Characters..... *none*.....  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

## Fasting



Time.	1	2	3	4	5	6	7	8	9
Notes:-	Initial effect of one Grachm Aluminium Hydroxide was to control the acid for over two hours without any stimulant effect. The result was not so happy in the second part of the test where the effect was but little better than that of the milk feeds alone.								



## CASE NO. 18.

MR.C.T.

Aged 67.

Complaint. Epigastric pain coming on half an hour after food.

Duration. Two years.

Examination. Clinically -High epigastric tenderness rigidity and hyperaesthesia, especially on the right side

Test Meal - see chart.

Faeces - no occult blood.

Barium Series -"marked duodenal ulcer deformity";

Diagnosis. Duodenal ulcer.

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

I.Effect of antacids( I drachm) on three hour test meal.

In the control the acidity did not rise above the normal limits but it tended to remain high towards the end of the test.Magnesium Trisilicate's effect lasted for 90 minutes, Sippy No.2. for 60 minutes ,and Aluminium Hydroxide for 45 minutes. The first two were followed by a small secondary rise in acidity.

II.Effect of antacids (gr.40) on nine hour test with hourly 3oz.milk feeds.

The control showed the inadequacy of the milk feeds as antacid in this case. All three antacids kept the "free" acid at a low level but only Aluminium Hydroxide completely controlled it. Sippy No.2. was the next best .

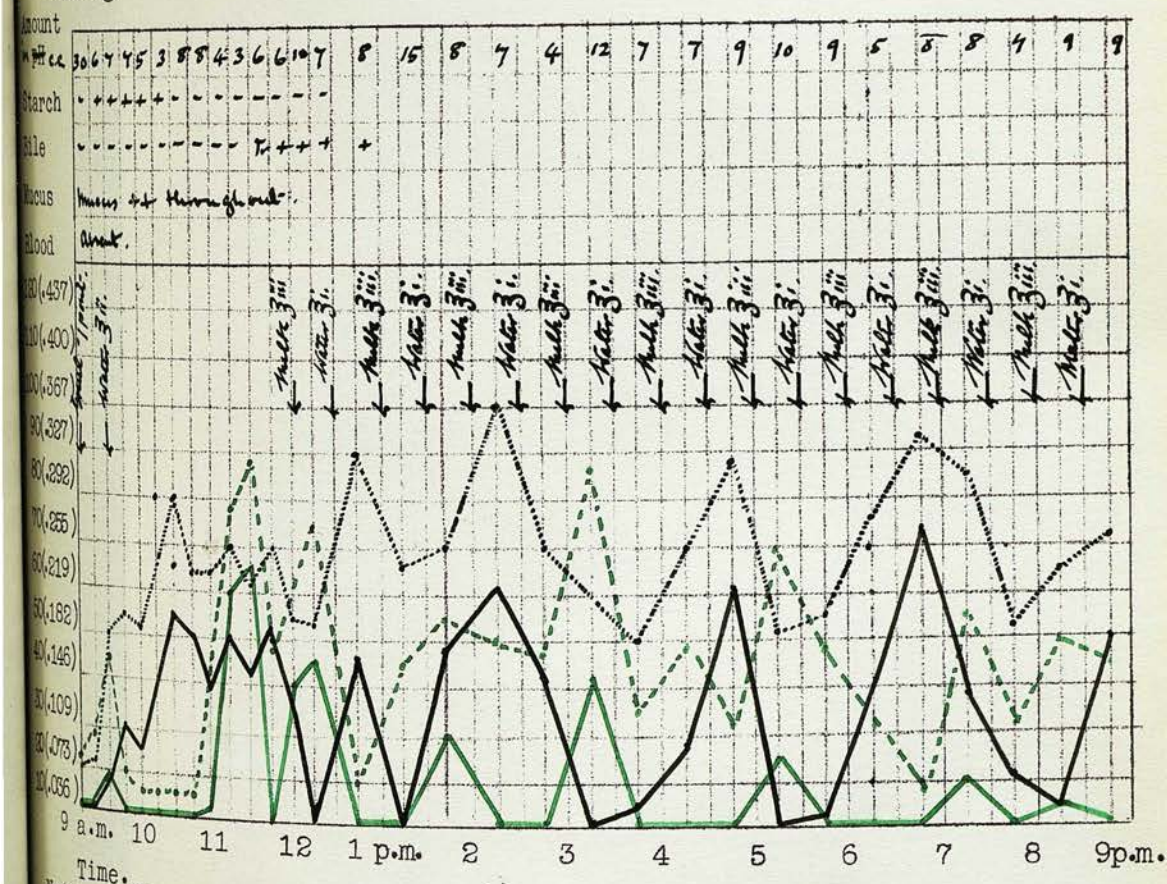


Case No. 18.  
 Name Mr. C. T.  
 Age 67.  
 Date 8th Feb. 1938.  
 Diagnosis Duodenal Ulcer.  
 Substances given:- Milk - as indicated below.  
 A. "Food". None. Water as indicated below.  
 B. Antacid(s). 30 c.c.  
 Fasting juice. Amount. 30 c.c.  
 Special Characters. Mucus. Excessive.  
 Acidity, etc. (See first column below.)

— represents free HCl.

..... represents total acidity.

Fasting



Notes:- Control curves compared with those of Magnesium Trisilicate. Low acidity of fasting juice - probably due to some extent (Green.) absorption by excessive mucus; good acid response to gruel, producing "normal" result; excellent initial neutralisation of acid by milk followed by stimulation so that subsequent milk feeds were quite inadequate to deal with high acid secretion produced.

Magnesium Trisilicate (1 drachm) controlled the acidity for over one and a half hours the subsequent rise exceeding slightly the highest point reached in the control.

In the second part of the test the "free" acidity was fairly well controlled but reached 32 points at 3.15 p.m.



# ANALYSIS OF GASTRIC CONTENTS.

166.

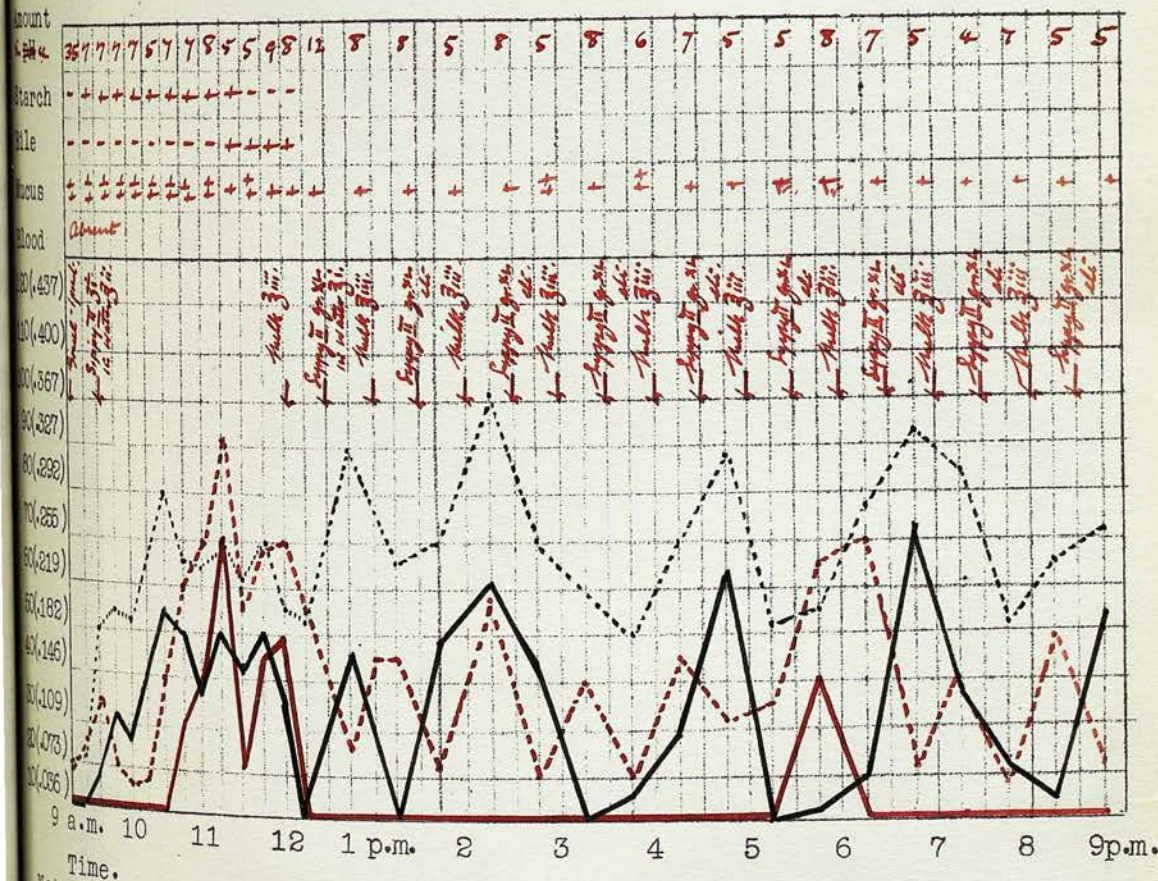
TEST WITH SIPPY POWDER NO. 2. (CONTROL- BLACK.)

Case No. 18.....  
 Name..... MR. C. T.....  
 Age..... 67.....  
 Date..... 10th. Feb. 1938.....  
 Diagnosis..... Duodenal Ulcer.....

Substances given:-  
 A. "Food". Gruel and milk - as indicated.  
 B. Antacid(s). Sippy No. 2. Powder - as indicated.  
 Fasting juice. Amount..... 35..... c.c.  
 Special Characters..... Mucus excessive.  
 Acidity, etc. (See first column below.)

..... represents free HCl.  
 ..... represents total acidity.

Fasting



Notes:-  
 "Free" acid neutralised for One hour following a  
 dose of one drachm of Sippy Powder: there was a moderate second  
 rise. In the second part of the test at only one point was  
 complete neutralisation not achieved: a very satisfactory result.



# ANALYSIS OF GASTRIC CONTENTS. MAGNESIUM TRISILICATE TEST.

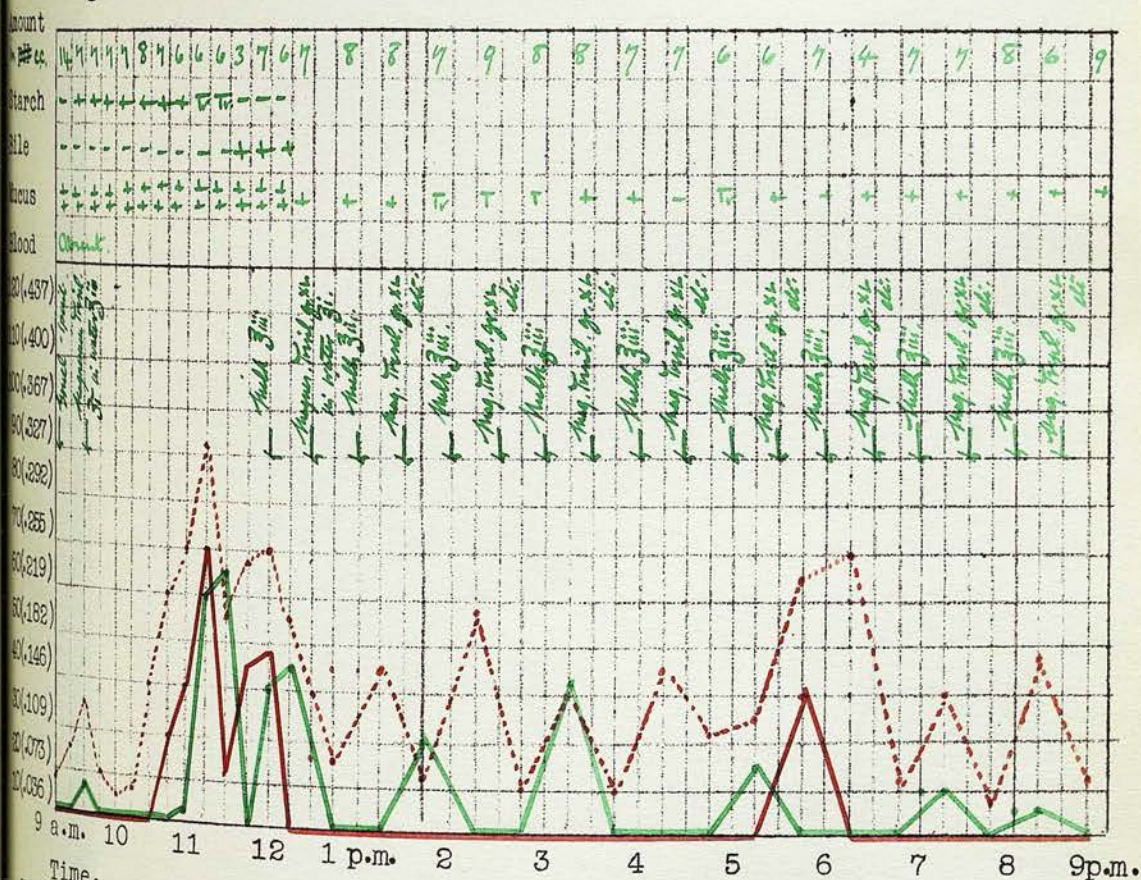
167.

Case No. 18.  
Name..... MR.C.T.  
Age..... 67..... Date. 12th Feb. 1938.....  
Diagnosis..... Duodenal Ulcer.  
Substances given:-  
A. "Food". ... AS INDICATED.....  
B. Antacid(s) Magnesium Trisilicate. .. as indicated.  
14 cc.  
Fasting juice. Amount..... c.c.  
Special Characters..... None.....  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:-

This shows that one drachm of Magnesium Trisilicate neutralised the acid for 30 minutes longer than the corresponding dose of Sippy Powder No.2. Both remedies were followed by a similar secondary acidity rise which exceeded the control by a small amount.

In the second part of the test both powders were fairly successful the Sippy Powder being slightly the better this time. (40 gr. doses hourly were being given.)



Case No. 18. Aluminium Hydroxide Test.

Name..... Mr. C. T. ....

Age..... 67. .... Date..... 14th. Feb. 1938, ....

Diagnosis..... Duodenal Ulcer, ....

Substances given:- Gruel and milk feeds - as indicated.

A. "Food". .... Aluminium Hydroxide ....

B. Antacid(s). ....

Fasting juice. Amount..... 8. c.c. ....

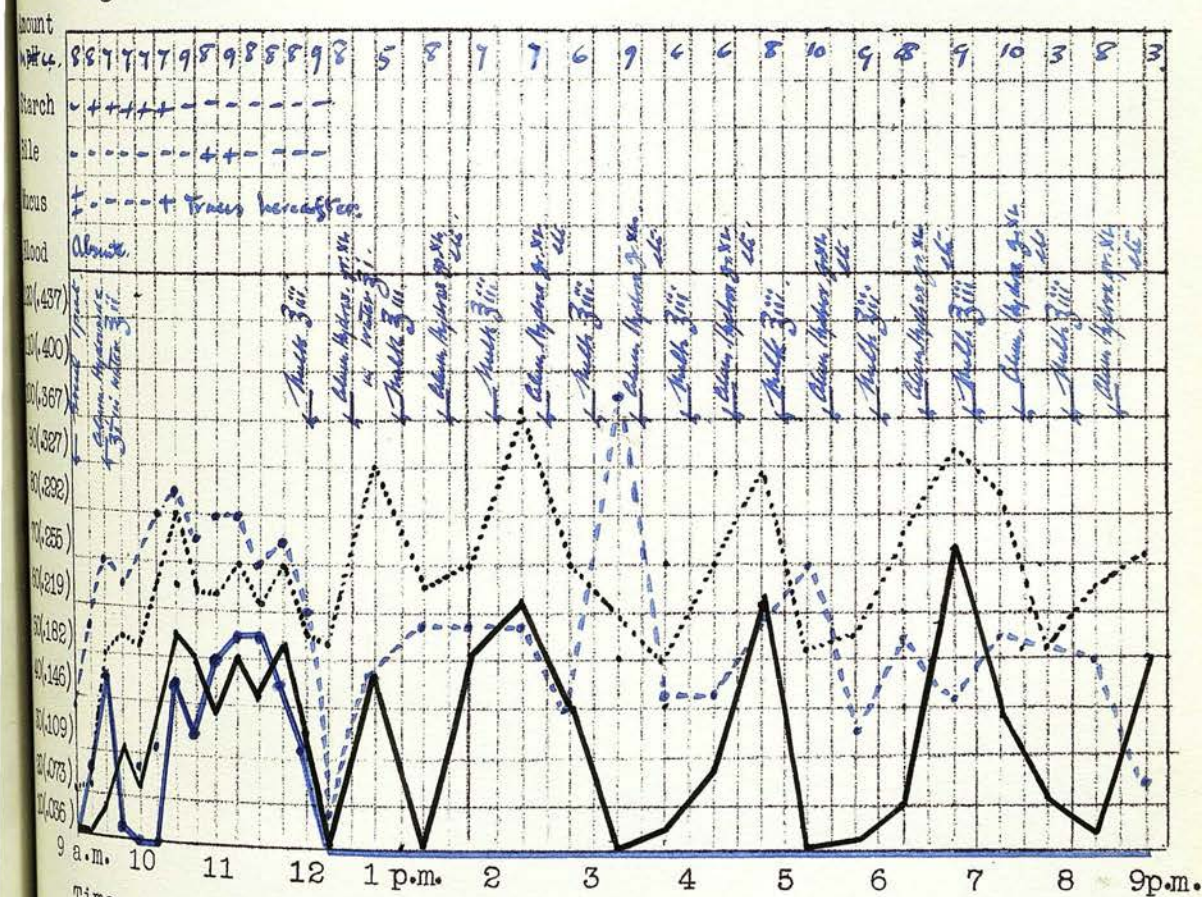
Special Characters.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Time.

Notes:-

Shows initial 45 - 60 minutes control by one drachm

Aluminium Hydroxide followed by no secondary rise in acidity ex-

ceeding the control as with the other two antacids.

Complete control throughout the remainder of the test.

was achieved by neither of the other two antacids.



## CASE NO. 19.

MR. J. L.

Aged - 40.

Complaint. "Numbness in the back of the right leg".

Duration. 5 weeks.

Examination. Negative as regards the alimentary system.  
on physical examination.

Test meal - mild degree of hyperacidity.

Diagnosis. Disseminated Sclerosis.

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.I. Effect of one drachm of antacids on three hour test meal.

Magnesium Trisilicate and Sippy No. 2 were found in this case of mild hyperacidity to exert a very small antacid action and both were followed by secondary acid stimulation, the former being less satisfactory than the latter in both respects. Aluminium Hydroxide was much the best and affected acidity for almost two hours and was followed by no stimulant effect.

II. Effect of antacids on nine hour test with 3oz. milk feeds and 40.gr. doses of powders hourly.

In this part of the test none of the three powders succeeded in completely controlling "free" acidity but Sippy No. 2 was by far the least successful in this respect. The other two were fairly good, Magnesium Trisilicate being rather the better.



"Control" Test.

No. 19.....

Mr. J. L.

Date. 28<sup>th</sup> Feb., 1938.

Diagnosis..... Disseminated Sclerosis.

Substances given:-

A. "Food". Gruel and milk feeds - as indicated.

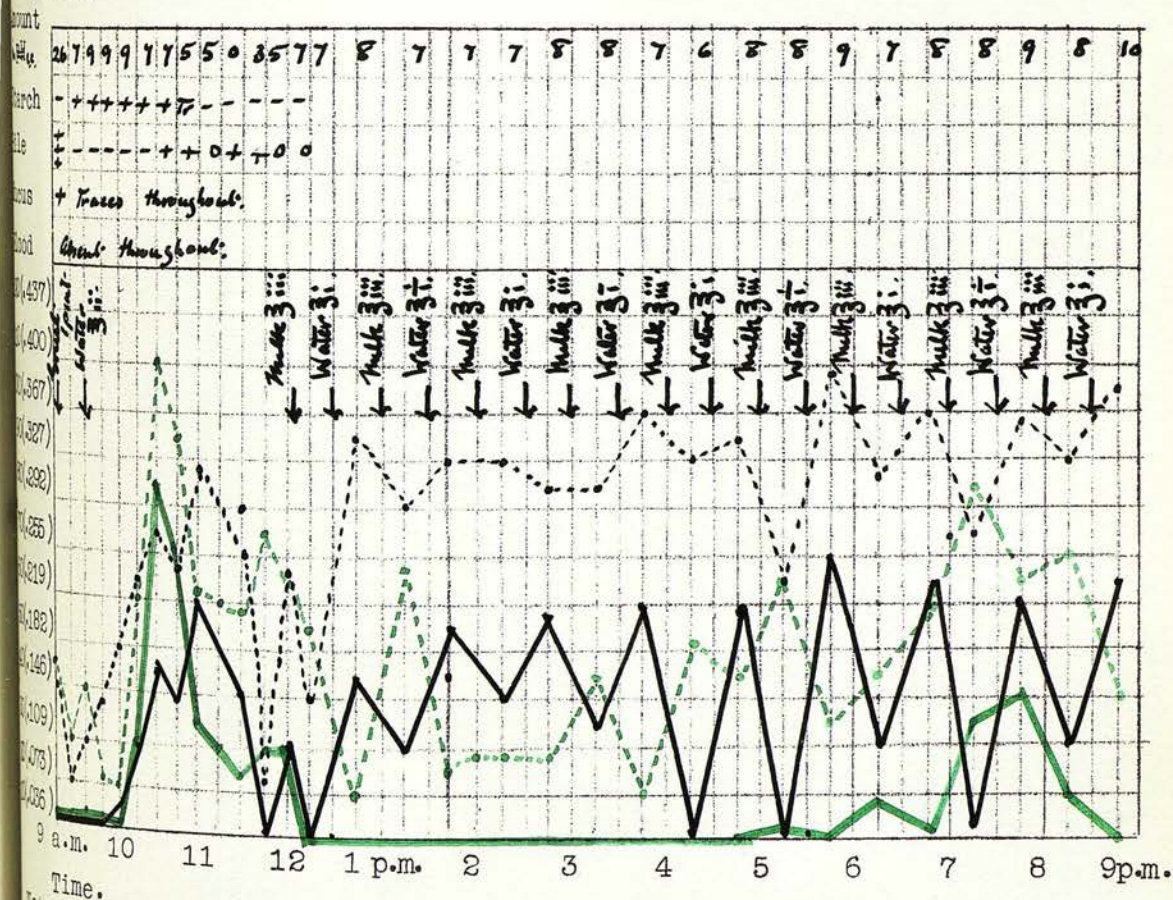
B. Antacid(s). none; but milk.

Fastest juice. Amount..... 26..... c.c.  
 Special Characters..... none.  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Time.

Notes:-

In this case of slightly high acidity which was not controlled effectively by the small milk feeds, it can be seen that a drachm of Magnesium Trisilicate had little if any effect in reducing this acidity but was followed by a marked secondary secretion which, however, soon fell below the level of the control. (It is possible that the antacid had not become properly mixed with the stomach contents till the later part of the test.)

With milk feeds, the control was almost complete.



No. 19.....

Sippy Powder, No. 2.

Mr. J. L.....

Date. 5<sup>th</sup> March, 1938.

Diagnosed Scleritis

stances given:-

A. "Food". *Food and milk feeds - as indicated.*B. Antacid(s). *Sippy No. 2 - initial dose 1 - 1 drachm.  
- hourly doses 1 - 40 grains*

ting juice. Amount.... 26..... c.c.

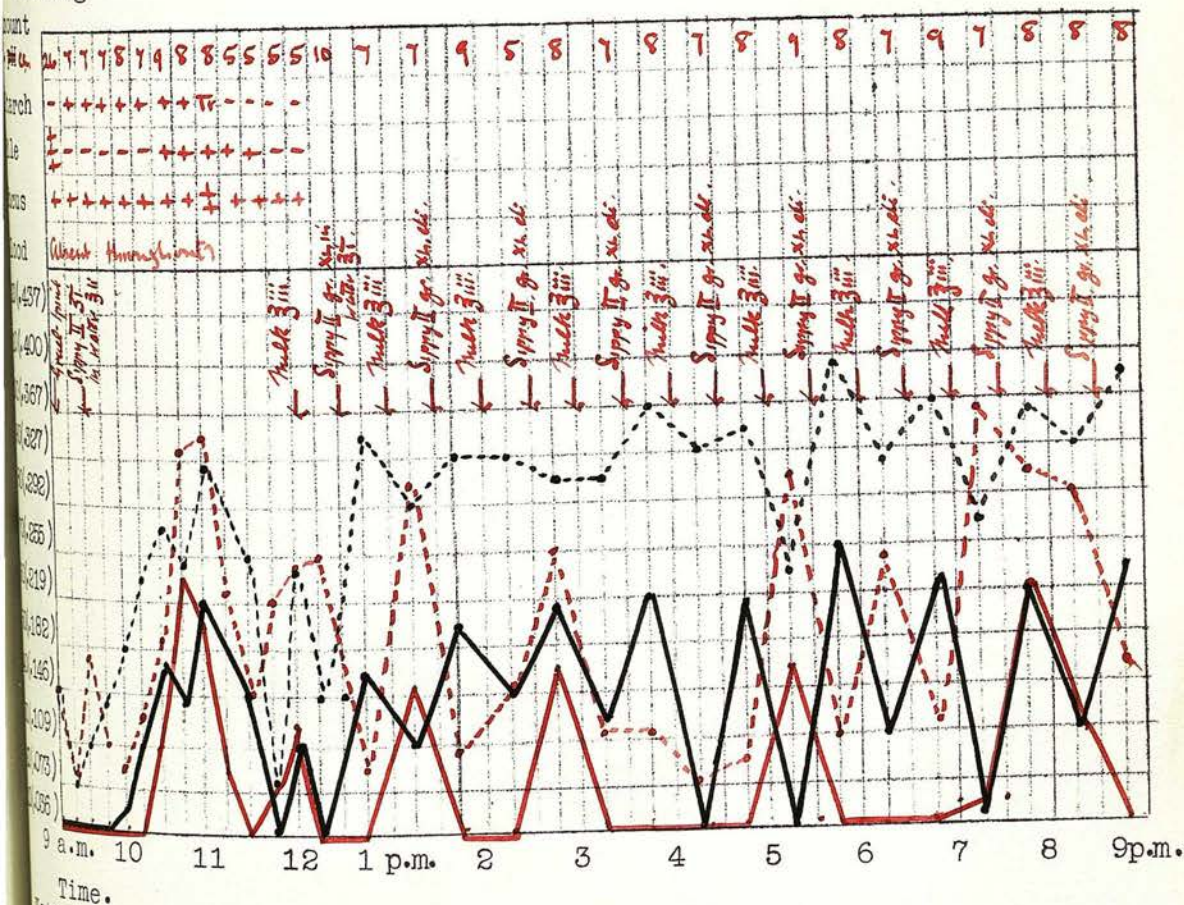
Special Characters..... *none*

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Pasting



Notes:- Some antacid influence is evident for about 45 minutes following the initial I drachm dose but when the control values are considered the effect is slight and was succeeded by a secondary rise in acidity.

With milk feeds control was not satisfactory since acidity rose above 30 points on four occasions and once reached 50 points.



e No. . . 19 . . . . .

Mr. S. W.

Date.. 2<sup>nd</sup> March, 1938.

## Disseminated Sclerosis

stances given:-

es given:-  
A. "Food". Gruel and milk feeds - as indicated.  
B. Antacid(s). Magnesium trisilicate - initial dose - 1 drachm.  
- hourly doses - 1/2 drachms.

sting juice. Amount..... 25 ..... c.c.

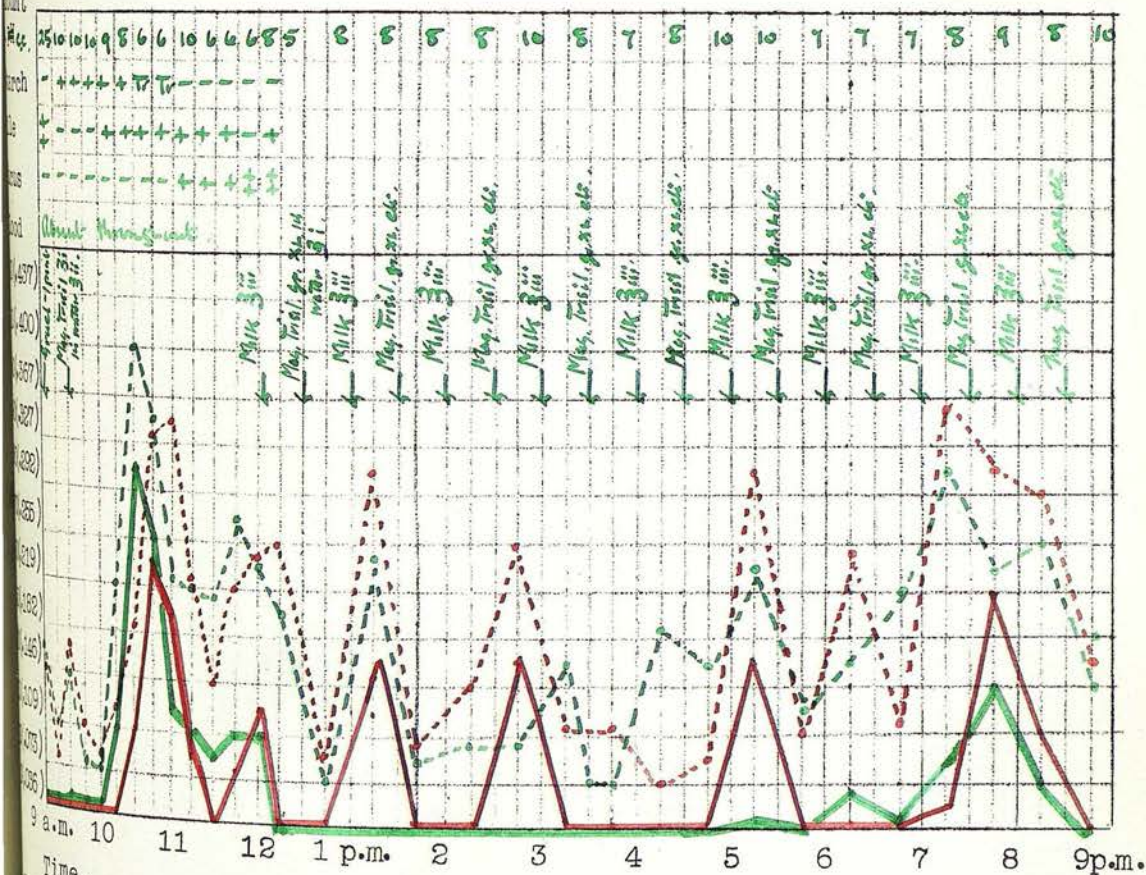
Special Characters.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Time. 11 12 1 p.m. 2 3 4 5 6 7 8 9 p.m.  
Notes:- An unusual effect was obtained in this case for the ant-  
influence (slight in both cases) lasted longer with Sippy No.2  
with Magnesium Trisilicate and was followed by a smaller second-  
stimulant action.

Magnesium Trisilicate's action must be considered the more violent in the second part of the test.



Case No. 19.....

No. .... Date. 3<sup>rd</sup> March, 1938.

distances given:-

distances given:-

A. "Food". *Spiced corn with peas - as shown*

B. Antacid (酸). Aluminum Hydroxide = 氢氧化铝

Netting juice. Amount.....<sup>25</sup>..... c.c.

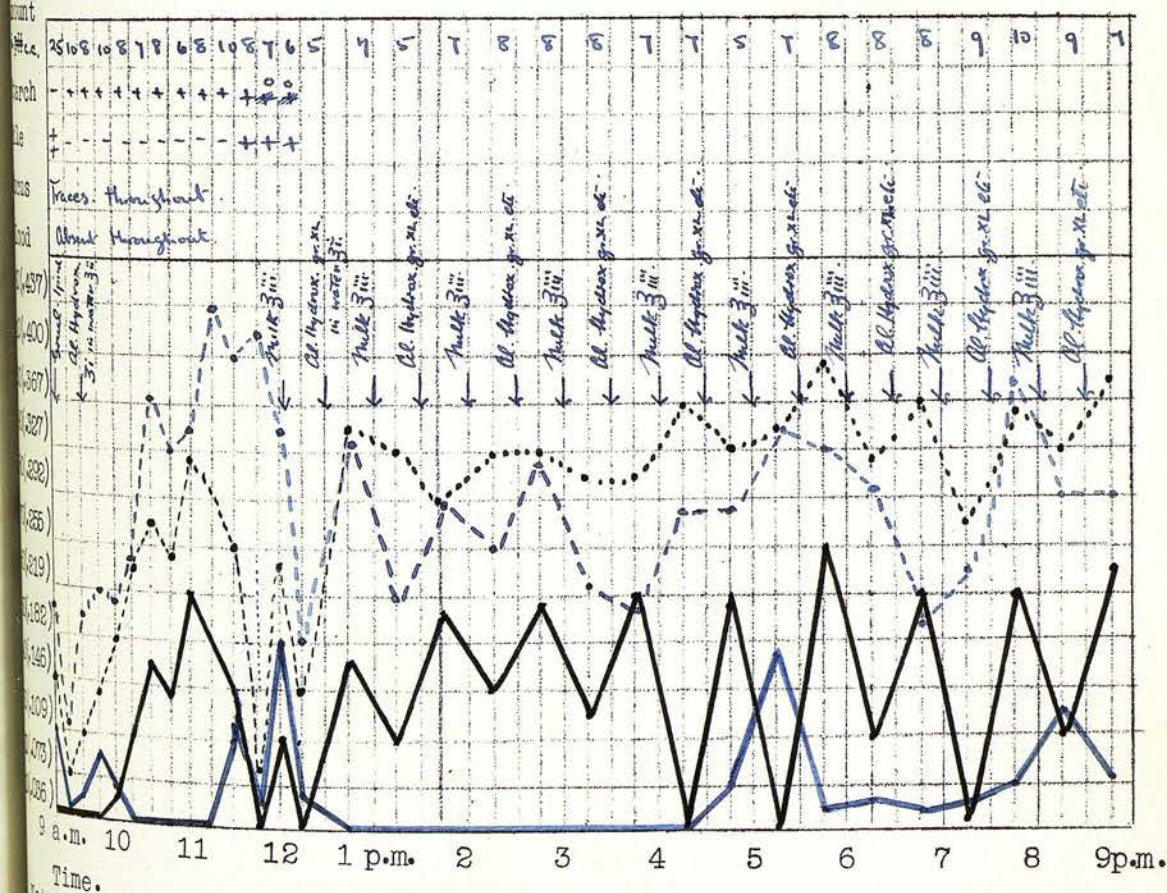
Special Characters.....<sup>hand</sup>

Acidity, etc. (See first column below.

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- Excellent antacid effect of Aluminium Hydroxide(I drachm) influencing the "free" acidity for almost two hours and not followed by any stimulant effect may be noted.

Although acid was present from time to time in the remainder of the test control was fairly satisfactory except at one point where "free" acid was 38 points.

## CASE NO. 20.

MR. W. H.

Aged - 43.

Complaint. Epigastric pain two hours after food.

Duration. Two months.

Examination. Clinically - Epigastric tenderness only.

Test meal - Very slightly above normal.  
acidity.

Barium series - negative.

Faeces - no occult blood.

Diagnosis. "Simple gastritis".

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.I. Effect of antacids (1 drachm) on three hour test.

In this case of slight hyperacidity Magnesium Trisilicate exerted no demonstrable antacid action, Sippy No. 2 had some effect lasting 45 - 60 minutes, while Aluminum Hydroxide's was rather more than 90 minutes. All three were followed by a marked secondary acid secretion. This is somewhat unusual and may in part be due to a rise in the control acidity as treatment was proceeding,, but at the same time the initial specimens gave very similar results on all but the last day of the tests, and so the remainder would probably have been the same had no antacids been given.)

II. Effect of the antacids on nine hour test.

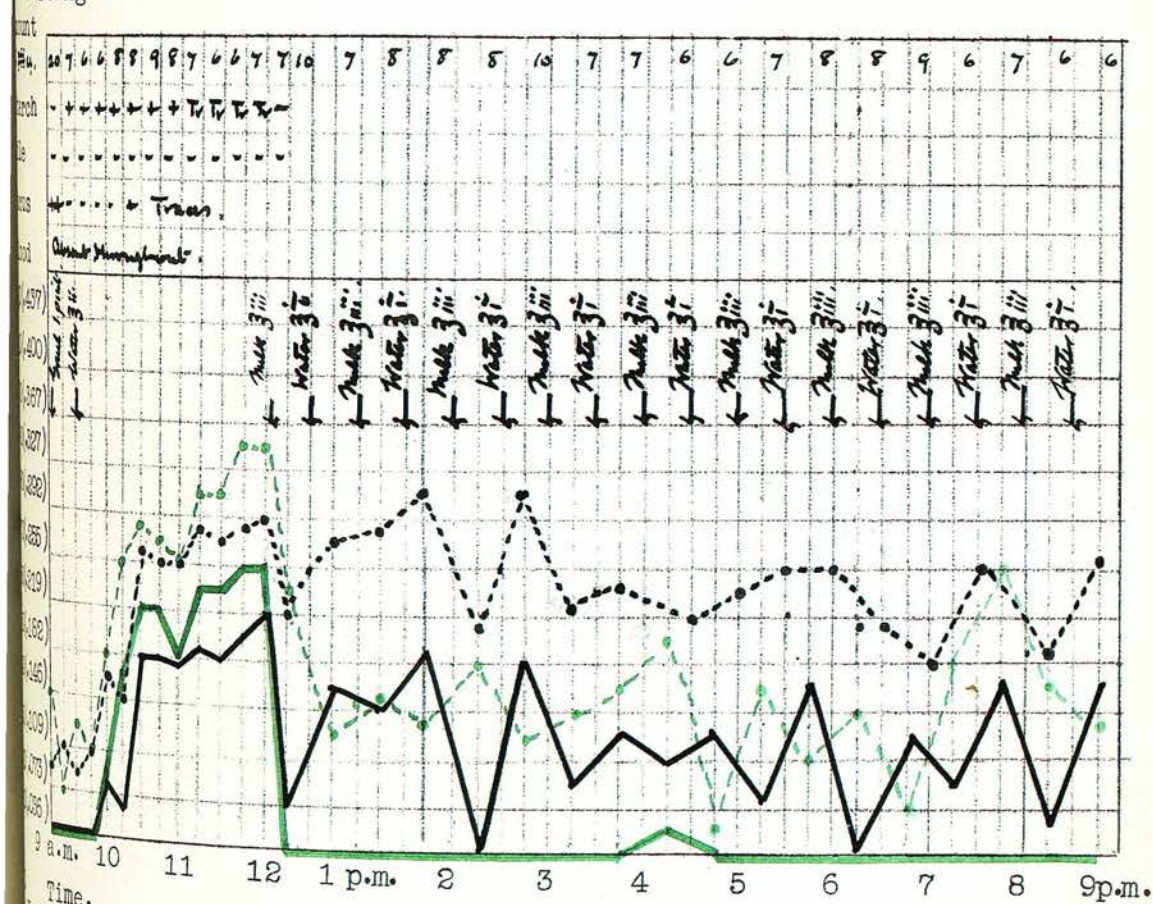
With milk feeds of three ounces hourly acidity was not controlled although not reaching high levels, but with addition of 40. gr. doses of the above antacids between the feeds control was almost complete and quite satisfactory in every case.



No. 20.....  
 Mr. W. H......  
 Date 15<sup>th</sup> Feb., 1938......  
 "Jejun's Gastritis".....  
 Antacids given:-  
 A. "Food". Bread and milk - as indicated......  
 B. Antacid(s). none; water as indicated......  
 Fasting juice. Amount.....20..... c.c.  
 Special Characters.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.  
 ..... represents total acidity.

Fasting



In this case of mild hyperacidity practically no antacid effect can be discerned after 1 drachm of Magnesium Trisilicate which was apparently followed by a secondary stimulation of the acid secretion it aimed to control.

With milk feeds and hourly doses of antacid control was practically complete, while milk feeds alone permitted "free" acid to be present almost the whole time (not usually at a very high level).



Case No. 20.....

Mr. L. H. ....

Date. 19<sup>th</sup> Feb. 1938.

Diagnosis. "Gastritis".....

Substances given:-

A. "Food". Small meal with fluids as indicated.....

B. Antacid(s). Sippy Powder No. 2. as indicated.....

Fasting juice. Amount. 14..... c.c.

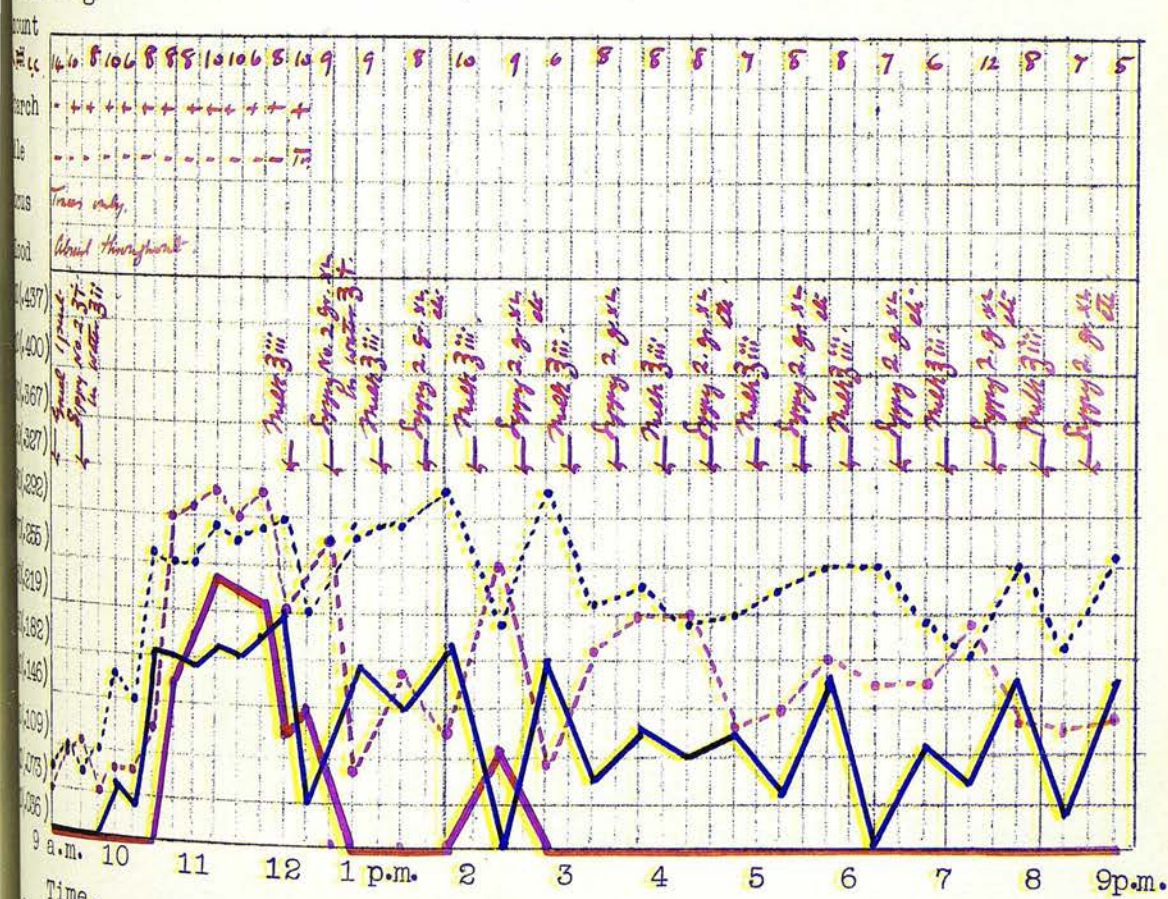
Special Characters.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting





No. 20.....

Mr. W. H. ....

Date. 17th Feb. 1938.

Diagnosis..... Simple Gastritis .....

Substances given:-

A. "Food". Gruel and milk - as indicated .....

B. Antacid(s). Magnesium Trisilicate in water - as indicated .....

Antacid juice. Amount..... 24..... c.c.

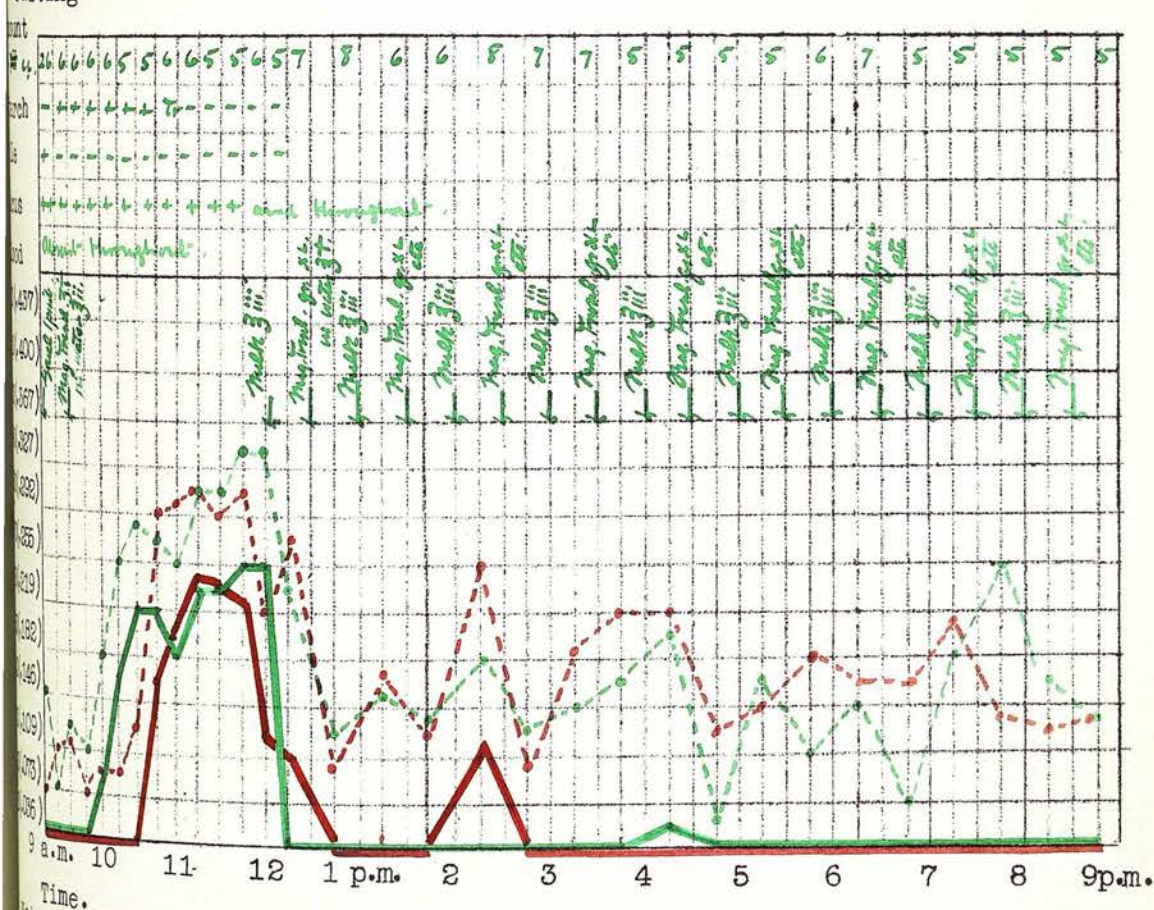
Special Characters.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting





Y-axis labels (mg. %): 9, 109, 146, 182, 219, 255, 292, 327, 367, 400, 437, 457.

X-axis labels (Time): 9 a.m., 10, 11, 12, 1 p.m., 2, 3, 4, 5, 6, 7, 8, 9 p.m.

Legend:

- Spinal fluid (solid black line)
- CSF (dashed blue line)
- Blood (dotted black line)

Annotations on the graph:

- Spinal fluid: 11 a.m. (x4), 12 p.m. (x4), 1 p.m. (x4), 2 p.m. (x4), 3 p.m. (x4), 4 p.m. (x4), 5 p.m. (x4), 6 p.m. (x4), 7 p.m. (x4), 8 p.m. (x4), 9 p.m. (x4).
- CSF: 11 a.m. (x4), 12 p.m. (x4), 1 p.m. (x4), 2 p.m. (x4), 3 p.m. (x4), 4 p.m. (x4), 5 p.m. (x4), 6 p.m. (x4), 7 p.m. (x4), 8 p.m. (x4), 9 p.m. (x4).
- Blood: 11 a.m. (x4), 12 p.m. (x4), 1 p.m. (x4), 2 p.m. (x4), 3 p.m. (x4), 4 p.m. (x4), 5 p.m. (x4), 6 p.m. (x4), 7 p.m. (x4), 8 p.m. (x4), 9 p.m. (x4).

Table of values (mg. %):

Time	Spinal fluid	CSF	Blood
9 a.m.	109	146	219
10	109	146	219
11	146	219	255
12	146	219	255
1 p.m.	146	219	255
2	146	219	255
3	146	219	255
4	146	219	255
5	146	219	255
6	146	219	255
7	146	219	255
8	146	219	255
9 p.m.	146	219	255

Table of 'Traces':

Time	Spinal fluid	CSF	Blood
9 a.m.	+	+	+
10	+	+	+
11	+	+	+
12	+	+	+
1 p.m.	+	+	+
2	+	+	+
3	+	+	+
4	+	+	+
5	+	+	+
6	+	+	+
7	+	+	+
8	+	+	+
9 p.m.	+	+	+

Control though not absolutely complete in the second part of the test was excellent for all practical purposes.



## CASE NO. 21.

M.P.R.

Aged -42.

Complaint. Epigastric pain two hours after food and relieved by a meal .----- 40 years.

Examination. Clinically - Tender to the left of the mid- line ; no rigidity.

Test meal - hyperchlorhydria.

Faeces -no occult blood.

Barium Series - "duodenal ulcer".

Diagnosis. Duodenal ulcer.

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

I. Effect of antacids on three hour test meal.

(Dose 1 drachm.)

In this case of hyperacidity Magnesium Trisilicate and Sippy No.2. each delayed the acidity rise by just over half an hour, while Alumunium Hydroxide appeared to exert some antacid influence for some two hours.

None of the powders was followed by any secondary acid stimulant action.

II. Effect of antacids on nine hour test with hourly

3oz. milk feeds and hourly 40 gr. doses of powder.

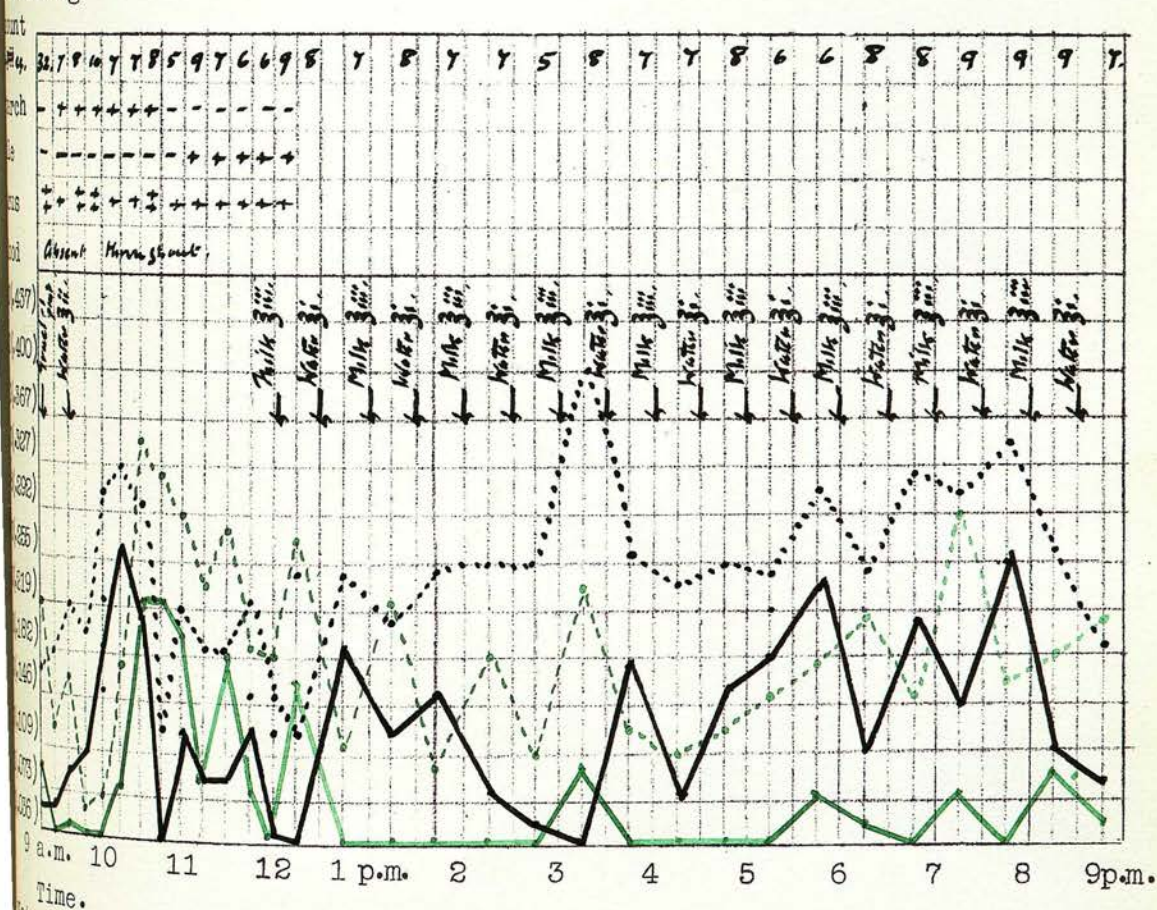
All three powders controlled the acid well but not completely, Aluminium Hydroxide being slightly the least effective.

Case No. 21..... "Control" Test.  
 Mr. P. R. ....  
 Date. 1<sup>st</sup> March, 1938.  
 Diagnosis..... Duodenal Ulcer.  
 Stomach given:-  
 A. "Food". .. Gruel and milk feeds: as indicated.  
 B. Antacid(=). .. none: last milk:  
 Stomach juice. Amount..... 32. .... c.c.  
 Special Characters..... none.  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Notes:- A case of hyperacidity which was not controlled by the milk feeds.

A drachm of Magnesium Trisilicate delayed the rise in acidity for 30 to 45 minutes only, but was not followed by a secondary rise in acid. With the milk feeds and powder the acidity never exceeded 18 points and was therefore satisfactorily controlled.



No. 21. Sippy Powder No. 2. Test.

Mr. P. R.

Date. 5th March, 1938.

Diagnosis. DUODENAL ULCER.

Quantities given:-

A. "Food". Gruel and milk feeds - as shown.

B. Antacid(s). Sippy No. 2 - (initial dose - 1 drachm.  
- hourly doses - 40 grains.)

Fasting juice. Amount. 20 c.c.

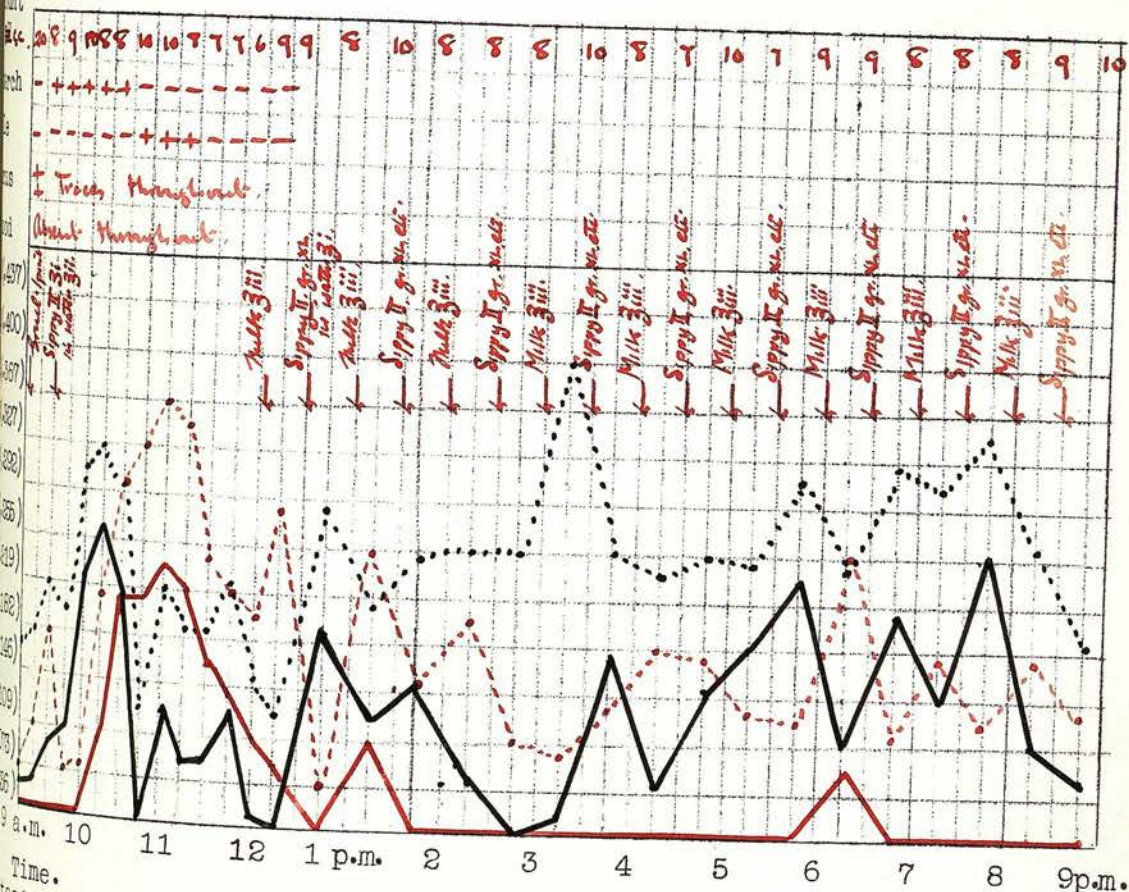
Special Characters. none.

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Sippy No. 2. (1 drachm) controlled the acidity for 40 minutes only and was not followed by a stimulation of secretion.

Almost complete control was achieved by 40 gr. doses only in the second part of the test.



## Magnesium Trisilicate Test.

Case No. 21.....  
 Mr. P. R.....  
 Age 42 years..... Date 3rd March, 1938.....  
 Diagnosis Duodenal Ulcer.....

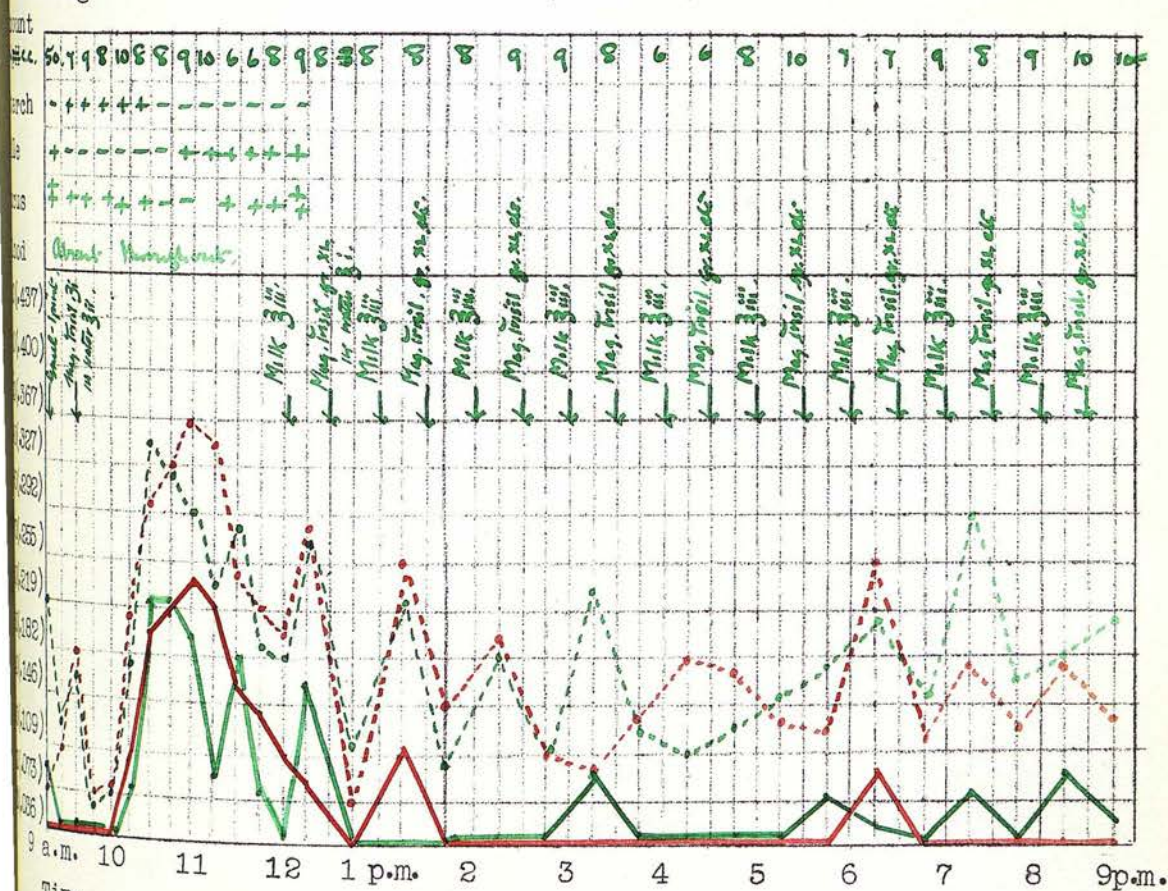
Substances given:-

- A. "Food". *Food and milk - as indicated*.....  
 B. Antacid(s). *Magnesium Trisilicate - as*.....

Antacid juice. Amount..... 50..... c.c.  
 Special Characters..... none.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.  
 ..... represents total acidity.

Pasting



Time.

Notes:-

Magnesium Trisilicate and Sippy NO. 2. showed an almost identical effect in this test.



Aluminum Hydroxide test.

Mr. P.R.

42.

Date. 7<sup>th</sup> March, 1938.

Duodenal Ulcer.

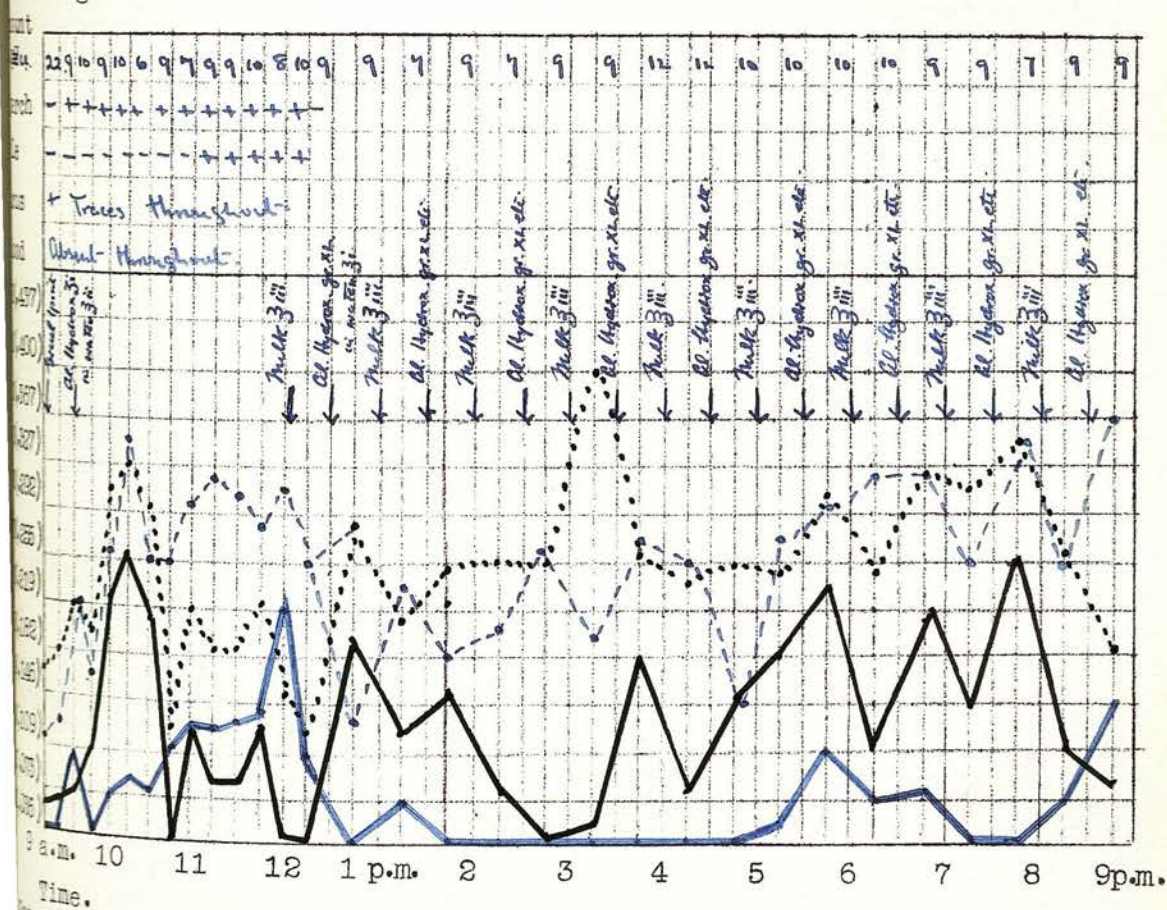
as given:-  
A. "Food". Food and milk - as shown.  
B. Antacid(s). Aluminium Hydroxide - 3i and gr. 40 - as shown.

Amount.....<sup>22</sup>..... c.c.  
Special Characters.....<sup>none</sup>.....  
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Aluminium Hydroxide appears to have exerted some control on the acidity for about two hours and was followed by no acid stimulation.

With milk feeds acid control though somewhat less com-  
-  
- than with the other two powders, was fairly satisfactory.

## CASE NO. 22.

MR. R.W.

Aged. - 63.

Complaints. - Cough, breathlessness on exertion, and upper abdominal discomfort after food...I year.

Examination .Clinically - Scar of previous operation for ? perforated peptic ulcer ; slight diffuse epigastric tenderness ;

Test meal - hyperacidity.

Faeces -no occult blood.

Barium series - negative.

Diagnosis . Aortic incompetence.

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

I. Effect of one drachm of antacids on three hour gruel test meal.

Aluminium Hydroxide had the most dramatic effect in that it neutralised the acid throughout the 2<sup>1</sup>/<sub>2</sub> hours of the test. Magnesium Trisilicate was next best with 1<sup>1</sup>/<sub>2</sub> hours effect and Sippy No.2. last with just over 45 minutes. The silicate was followed a stimulant effect which was greater than that of the Sippy Powder... an unusual effect.

II. Effect on the nine hour test of 40 gr. doses of the antacids hourly.

All three achieved complete "free" acid control where the hourly 3 oz. milk feeds had been quite ineffective.



"Control" Test.

Case No. 22.....

Mr. R. W. ....

63.....

Date... 14<sup>th</sup> March, 1938.....

"Aortic Incompetence".....

Distances given:-

A. "Food". *Small and milk feeds as shown.*.....B. Antacid( ). *none.*.....

Fasting juice. Amount..... 20..... c.c.

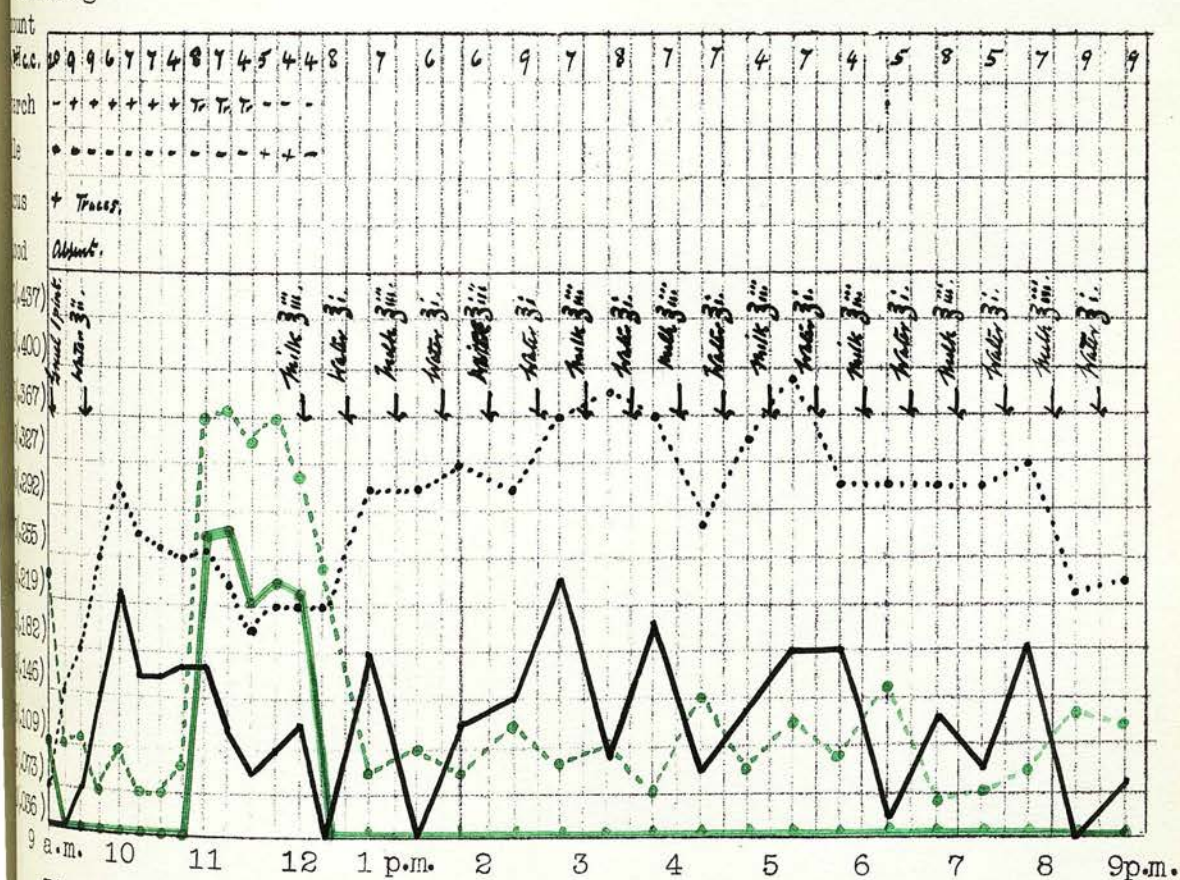
Special Characters.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Time.

Notes:- Almost 1½ hours acid control with initial dose of the drachm followed by some secondary rise in acidity in this case or hyperacidity.

In the remainder of the test the Magnesium Trisilicate completely neutralised the acid where the milk feeds alone failed.



## Sippy II. Test.

Mr. R. W.

Date... 20<sup>th</sup> March, 1938

"Acute Incompetence."

Distances given:-

A. "Food". *Gruel and milk feeds - as shown.*B. Antacid(s). *Sippy II. initial dose - 1 drachm.  
hourly doses - 40 grains*

Antacid juice. Amount..... 1.8 ..... c.c.

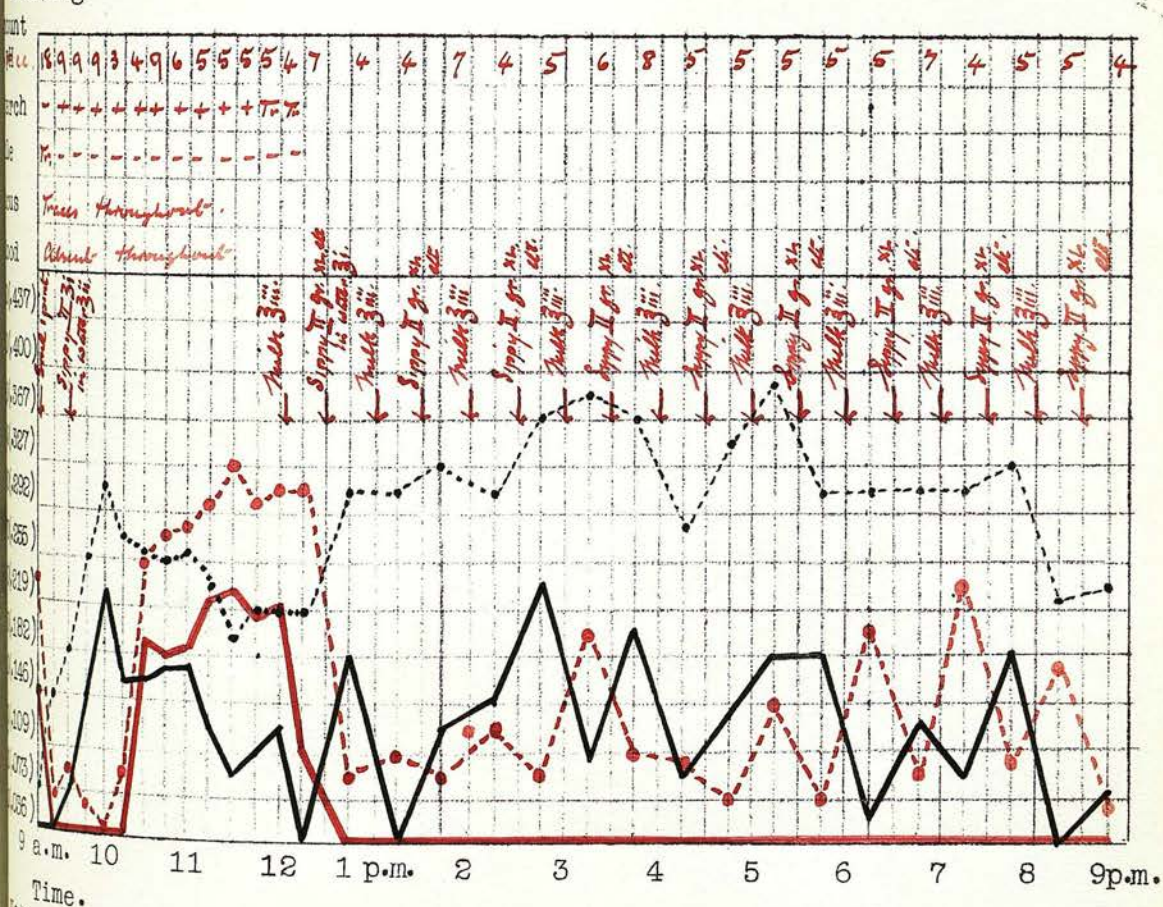
Special Characters..... *none*

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Time.

Notes:-

45 to 60 minutes control with initial dose only but no evidence of secondary stimulation effect.

Complete neutralisation was achieved in the second part of the test.



Magnesium Trisilicate Test.

No. 72.....  
 Name Mr. R. W......  
 Date 16<sup>th</sup> March, 1938.....  
 Diagnosis "Aortic Incompetence".....

Antacids given:-

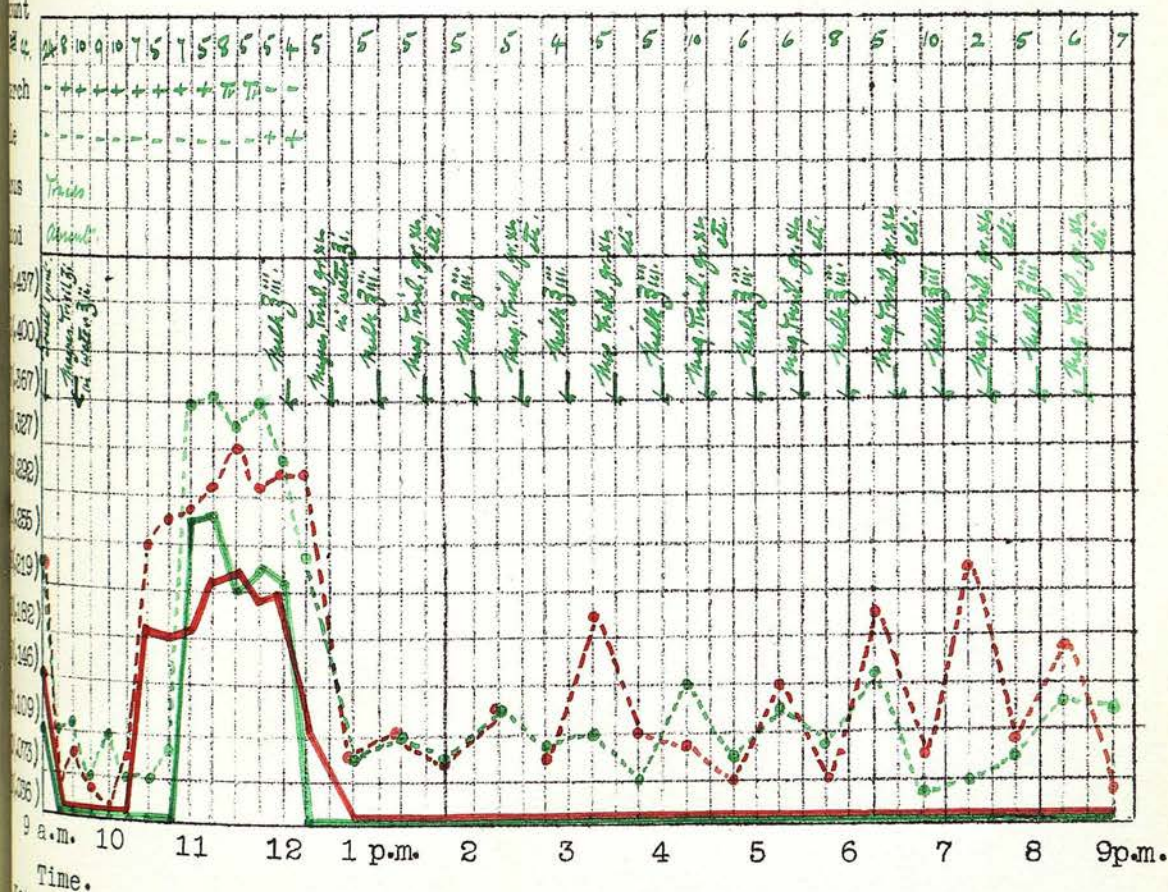
- A. "Food". Gruel and milk feeds - as indicated.....  
 B. Antacid(s) Magnesium Trisilicate - initial dose - 1 dram - hourly doses - 4 grains.....

Antacid juice. Amount 2h..... c.c.  
 Special Characters None.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Time.  
 Notes:- More prolonged but greater after stimulant effect of  
 Magnesium Trisilicate seen in this case.

Both antacids were quite successful in the second  
 part of the test.



No. 22..... Aluminium Hydroxide Test.

Mr. R.W. ....

Date 18<sup>th</sup> March, 1938.....

Diagnosis..... "Aortic Incompetence".....

Quantities given:-

A. "Food". Gruel and milk feeds - as indicated.....B. Antacid(s). Aluminium Hydroxide - initial dose: 1 drachm  
- hourly doses, 40 grains.

Fasting juice. Amount..... 20..... c.c.

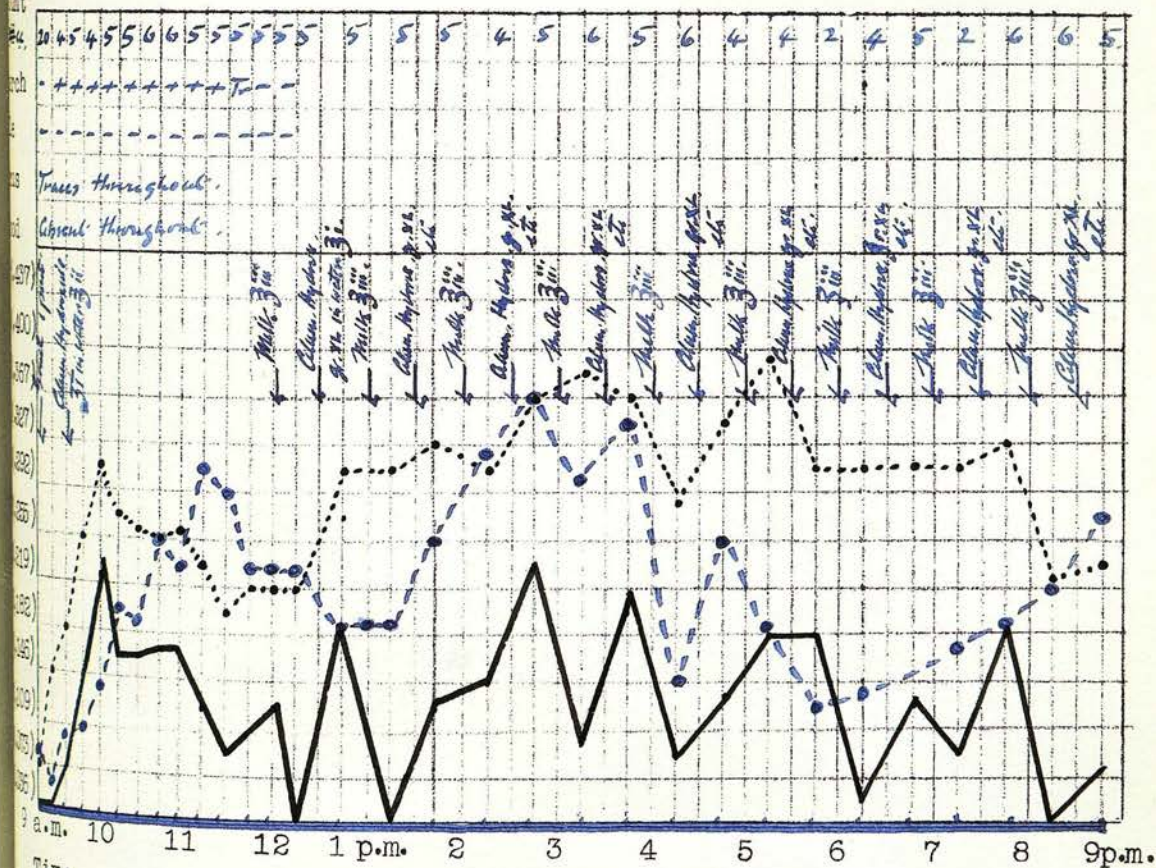
Special Characters..... none.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Aluminium Hydroxide's excellent effect in neutralising the "free" acid throughout the 2½ hours it was allowed to act is shown.

Complete neutralisation was achieved in the rest of the test.



## CASE NO. 23.

MR. D.J.

Aged - 29.

Complaint.- " Pains in the stomach relieved by the usual antacid powders".....I year.

Examination. Clinically - negative .

Stools- no occult blood.

Barium series - negative.

Test meal - hyperchlorhydria.

Diagnosis. Gastritis and hyperacidity.

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

Effect of one drachm of antacids on three hour test meal.

Magnesium Trisilicate controlled the acidity for  $1\frac{3}{4}$  hours Sippy No.2. for some 45 minutes and Aluminium Hydroxide produced an indefinite effect. None produced a stimulant action but with Sippy Powder the level of the control was much more quickly attained than with the other two powders.

II. Effect of the antacids on the nine hour test.

All three powders controlled the acid well but with Sippy No.2. the effect was not quite complete.

"Control" Test.

No. 23.....

Mr. D. J. ....

No. 29.....

Date 14<sup>th</sup> March, 1938.

Diagnosis..... Gastritis and hyperacidity: .....

Diet given:-

A. "Food". *Small: ant. milk feeds (3 oz.) hourly...*B. Antacid(s). *none*.....

Fasting juice. Amount..... 26:..... c.c.

Special Characters..... *none*.....

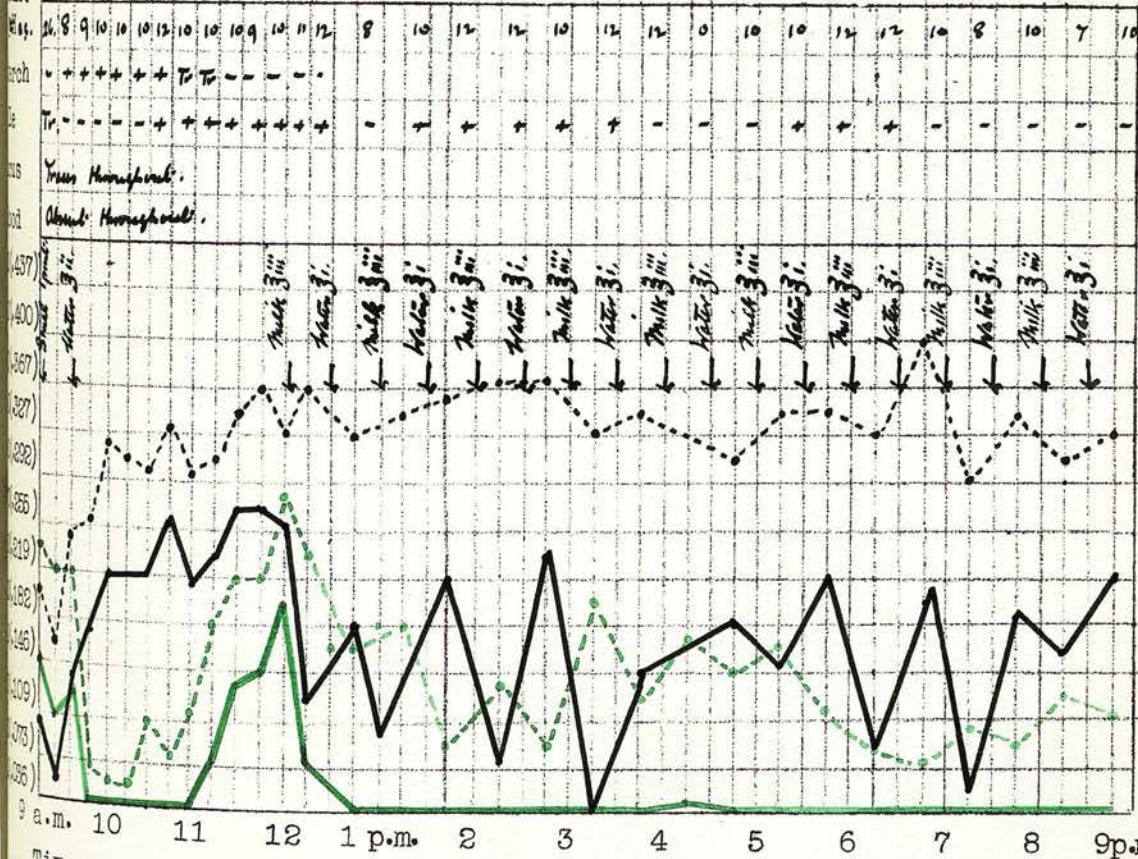
Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting

Amount



Notes:- Shows the excellent effect of Magnesium Trisilicate 1 drachm in controlling "free" acidity for 1½ hours with no stimulant effect afterwards in this case of hyperacidity.

In the remainder of the test milk feeds were quite inadequate but the powder controlled the acidity very efficiently.

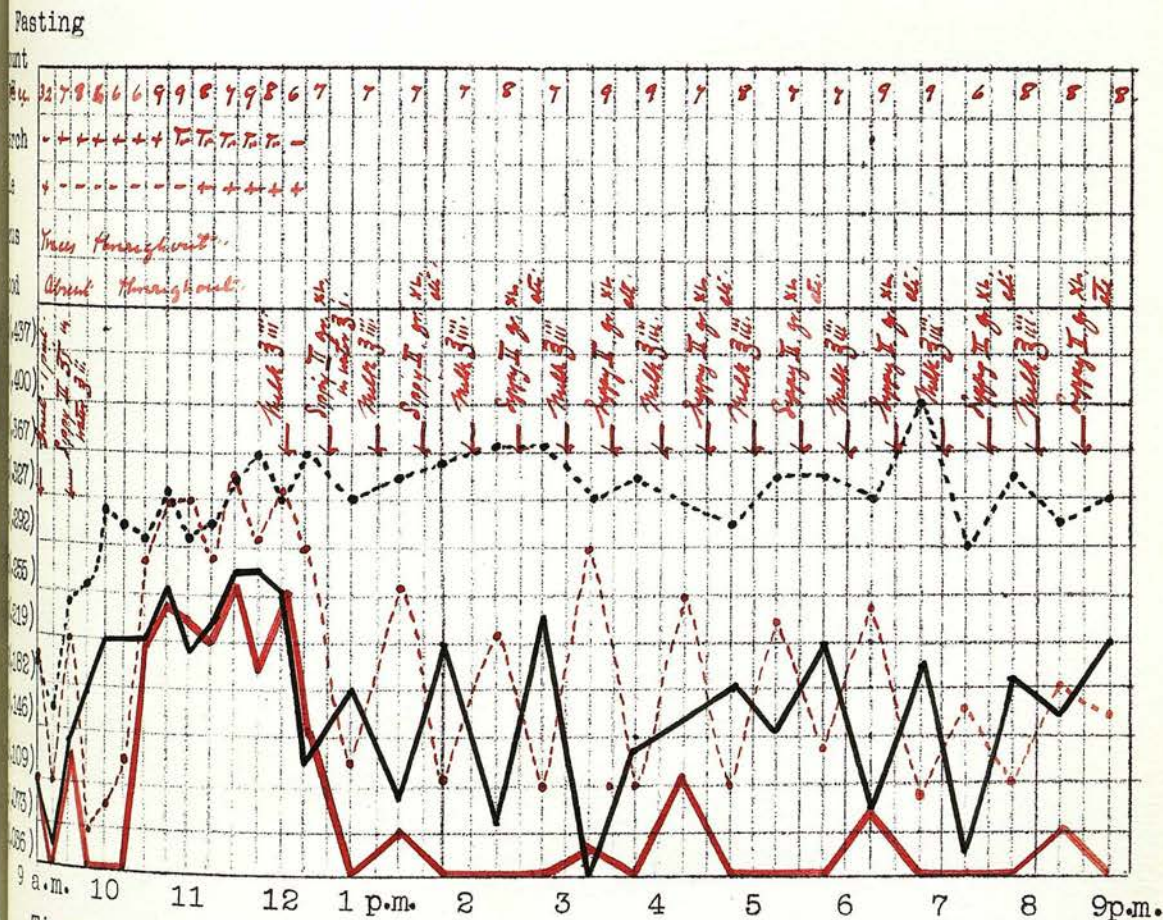


# ANALYSIS OF GASTRIC CONTENTS.

191.

No. *23*..... *Sippy Powder No. 2. Test.*  
*Mr. D. J.*  
 Date..... *18<sup>th</sup> March, 1938.*  
 Diagnosis..... *Gastritis and hyperacidity.*  
 Treatments given:-  
 A. "Food". .. *Gruel (1 pint) 1 and milk feeds - 3oz*  
 B. Antacid(s). *Sippy Powder, No. 2. - 100 grains*  
 Amount..... *32*..... c.c.  
 Special Characters.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.  
 ..... represents total acidity.



Time.  
 Notes:-  
 Sippy No. 2. Powder's transient effect can be seen in this case in the initial dose.  
 In the remainder of the test the effect was good but not complete.



*Magnesium Trisilicate Test.**No. 2: 5.*Date *16<sup>th</sup> March, 1938.**Gastritis and hyperacidity.*

stances given:-

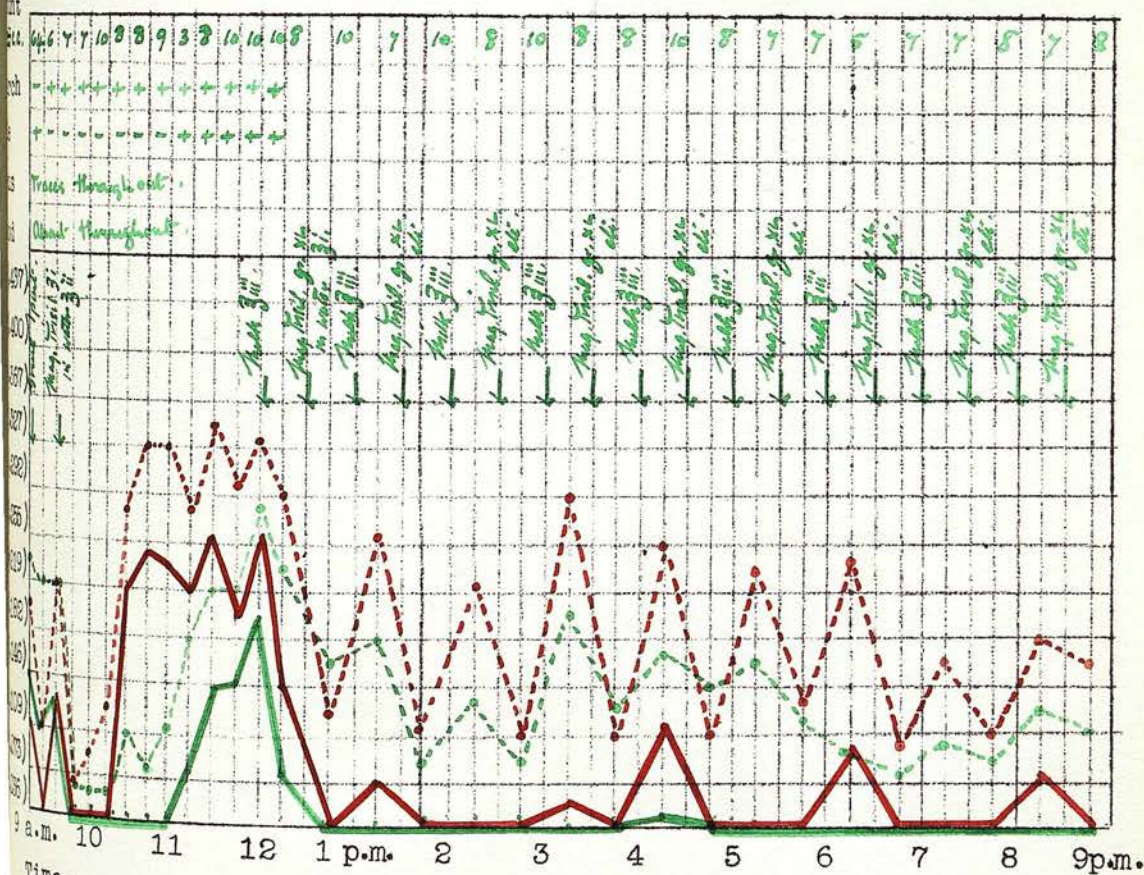
A. "Food". *Gruel (1 pint): milk feeds (3g) hourly.*B. Antacid(s). *Magnesium Trisilicate - Usual dose 1-1 1/2 c.c. hourly doses 1-40 grains.*ing juice. Amount *64*..... c.c.Special Characters..... *none*

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



Time.

Notes:-

Antacid effect lasted only some 45 minutes and was followed by marked secondary secretion of acid. with Sippy No 2

In the second part of the test a good control was achieved but this was not complete. with the Sippy Powder. In both parts of the test therefore Magnesium Trisilicate is the more satisfactory antacid.



### Aluminium Hydroxide Test.

No. 23. . . . .

Mr. D. J.

Date.. 20<sup>th</sup> March, 1938.

Gastritis and hyperacidity.

Instances given:-

A. "Food". Good and rich food, mostly (30%)...

B. Antacid(s). *Calcium carbonate, hydroxide, - initial dose! - 1 drachm.*

ing juice. Amount..... c.c.

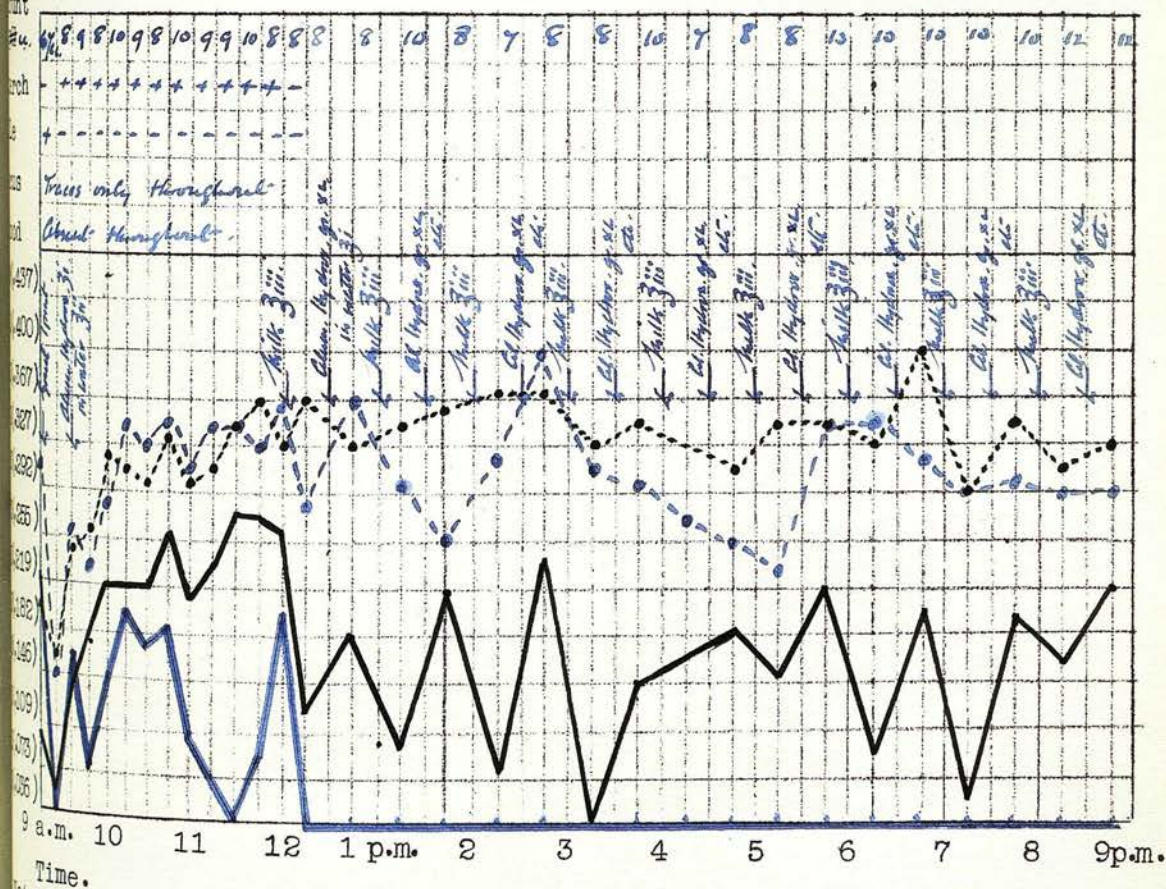
Special Characters..... *hmc* .....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

## Fasting



Notes:- A An incomplete effect of the initial dose of powder is shown and the fall in acidity some 75 minutes after administration may have been due to failure of the antacid to become diffused through the stomach contents. No stimulant effect is present.

Complete control was achieved in the remainder of the test.



## CASE NO. 24.

MR. J. P.

Aged - 74.

Complaints. "Vomiting blood" nine days prior to admission, this being followed by severe right epigastric pain for 8 hours.

No previous digestive trouble.

Examination. Clinically - Liver palpable 2" below the costal margin. --- otherwise negative.

Test meal - marked hyperacidity.

Faeces - no occult blood.

Barium series - irregularity at lower end of oesophagus - ? varices; no ulcer.

Diagnosis. Cirrhosis of the liver.

SUMMARY OF RESULTS OF GASTRIC CONTENTS' ANALYSES.

I. Effect of one drachm doses of antacids on three hour test meal.

In this case Sippy Powder No. 2. was most effective in controlling the acid for **2** hours; Magnesium Trisilicate came next with over 45 minutes effect, and Aluminium Hydroxide last with very little demonstrated effect at all. None caused a stimulant effect afterwards.

II. Effect of antacids in 40 gr. hourly doses in controlling acidity in nine hour test.

The milk feeds alone were not enough to control the acid but all three powders were very effective and produced no excessive effects. Aluminium Hydroxide only permitted "free" acidity to rise to 10 points at one pint only.



"Control" Test.

Mr. J. P.

Date 18<sup>th</sup> Feb. 1938.

Cirrrosis of the liver

stances given:-

A. "Food". *Equal (1 pint) : milk feeds 3g.*B. Antacid(=). *none but milk.*

ing juice. Amount.....14..... c.c.

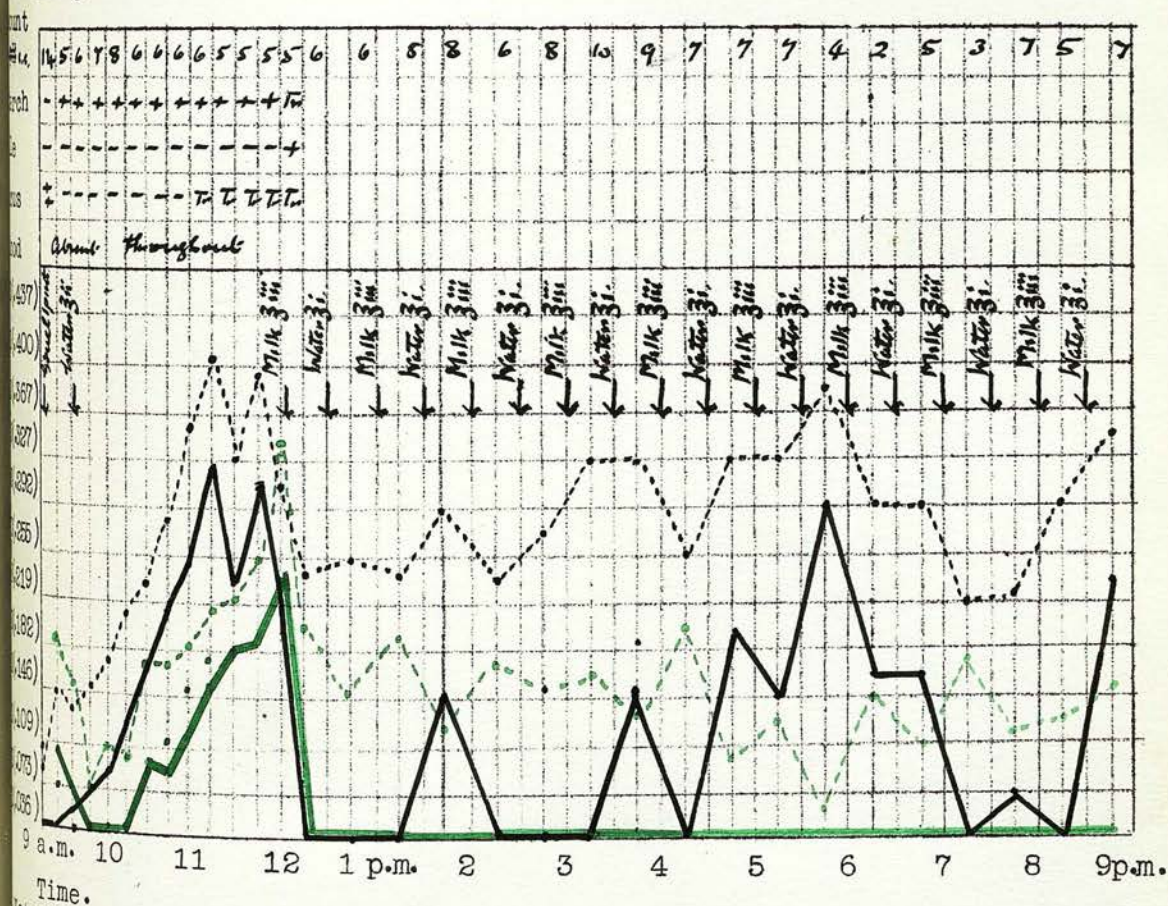
Special Characters.....*none*.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Pasting



Only 45 to 60 minute effect of single dose of I

of Magnesium Trisilicate, but no evident stimulant

effect in this case of marked hyperacidity.

Complete control in the rest of the test by the

when milk feeds alone were quite unsuccessful.

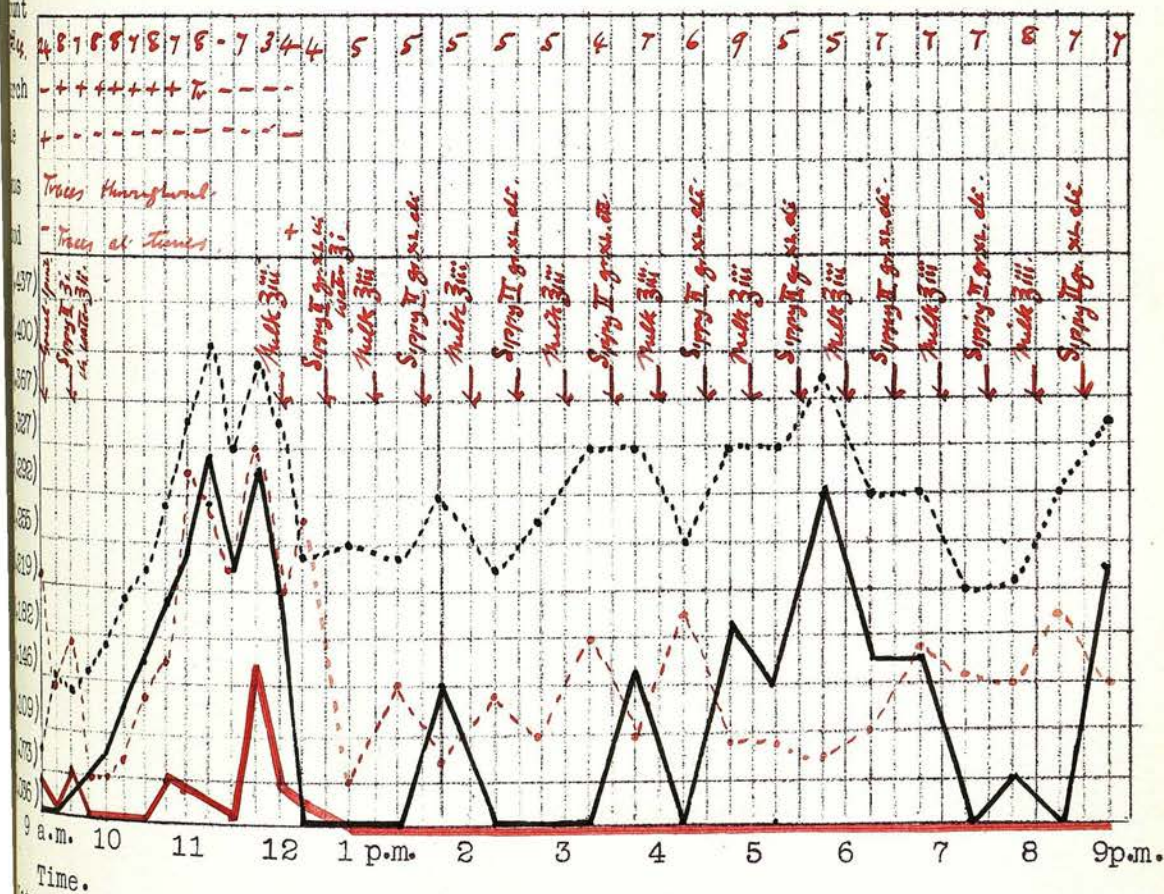


No. 24 :..... *Sippy Powder No. 2. Test.*  
 Date. *21<sup>st</sup> Feb. 1938.*  
 Name. *MR. J. P.*  
 Diagnosis. *Cirrhosis of the liver.*  
 Stomach contents given:-  
 A. "Food". *Gruel (1 pint); milk feeds (3 g.)*  
 B. Antacid(s). *Sippy Powder No. 2. - initial dose: - 1 drachm.  
 - hourly doses: - 40 grains*  
 Stomach juice. Amount. *24*..... c.c.  
 Special Characters..... *none*  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Pasting



Notes:-

Over two hours effect following a single dose of one drachm of Sippy Powder No. 2., with no stimulant action as a secondary effect.

Completely satisfactory control in the rest of the test.



Ms. J. P.

74:..... Date.. 19<sup>th</sup> Feb., 1938.

Leucophaea of the liver

stances given:-


A. "Food". Gruel (1 pint) + milk feeds (3-4) hourly

B. Antacid(s). Magnesium trisilicate - as indicated; initial dose - 1 dose, hourly doses - 40 grains

ing juice. Amount..... c.c.

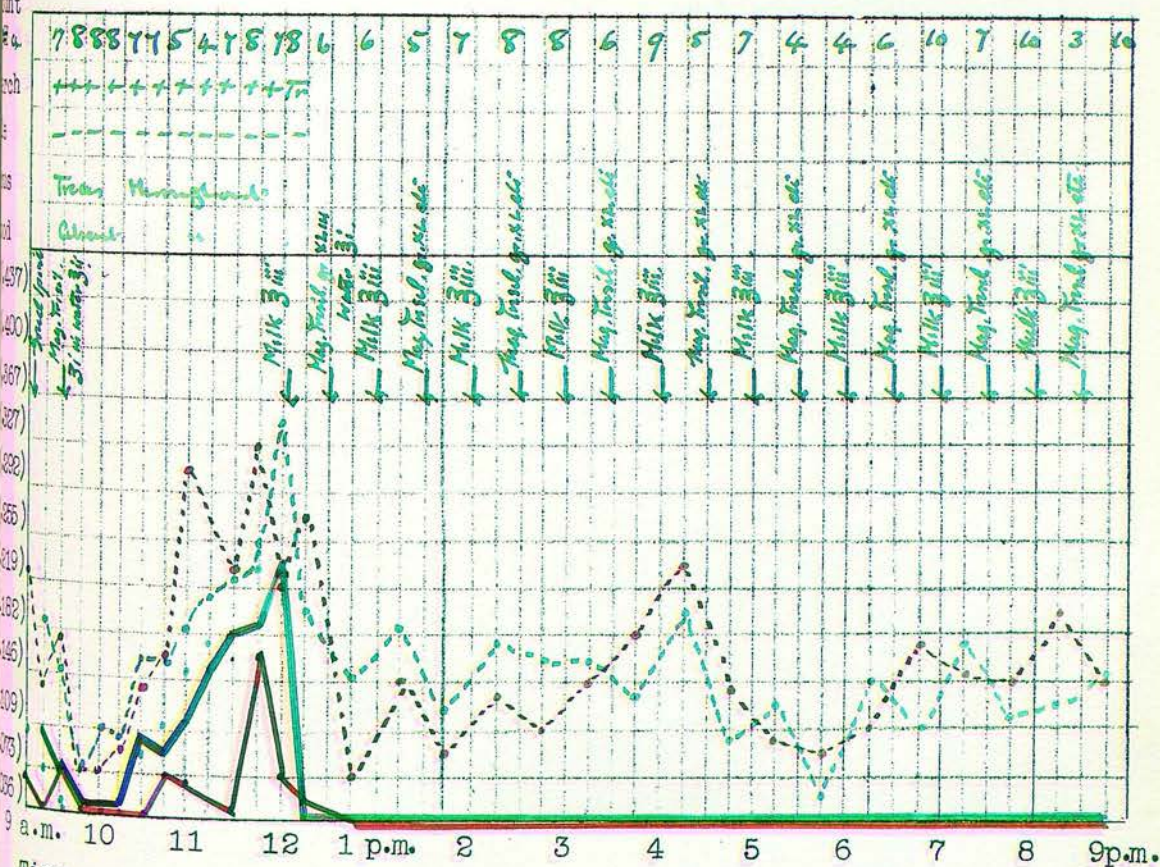
Special Characters.....*none*.....

Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

## Fasting



Time  
otes:-

Shows a case in which the Sippy Powder No.2. was

effective than Magnesium Trisilicate in a single large

Both powders were quite effective in the second part

## The test



No. 24..... Aluminium Hydroxide Test.  
 MR. J. P.  
 Date 24<sup>th</sup> Feb., 1938.  
 Diagnosis Biothesis of the liver.

stances given:-

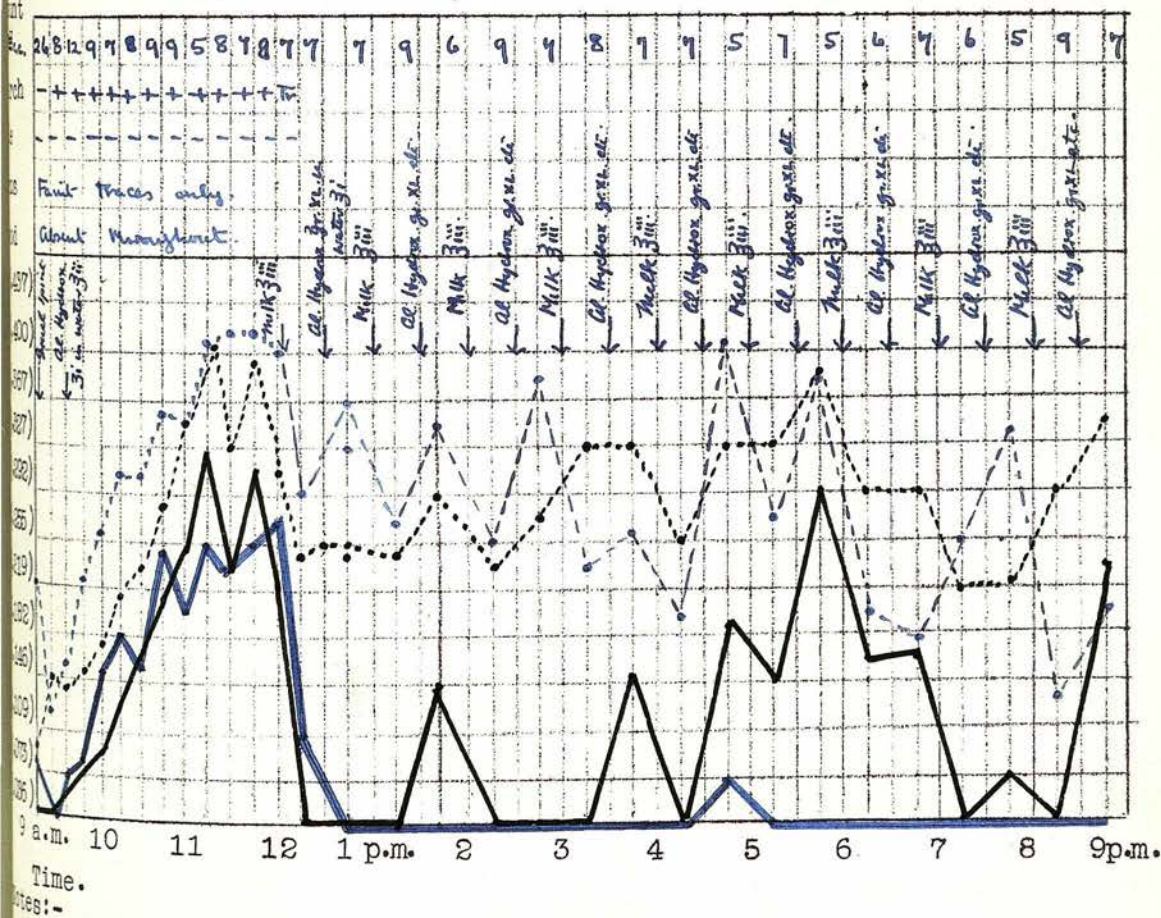
A. "Food". *Lyophil. and milk feeds (3oz.) - as shown.*  
 B. Antacid (s). *Aluminium Hydroxide: - initial single dose - 1 drachm.*  
*- hourly doses - 40 grains.*

ing juice. Amount..... 26..... c.c.  
 Special Characters..... none.....  
 Acidity, etc. (See first column below.)

..... represents free HCl.

..... represents total acidity.

Fasting



In this case Aluminium Hydroxide exerted but little effect in a single large dose.

When given hourly however it achieved almost as complete result as the two other powders.



## SUMMARY OF CHAPTER IV.

The results of the analysis of gastric contents studied over several twelve hour periods in the same patient when varying antacid medication was in progress as described in Chapter III is presented.

Twenty four cases were thus investigated, and the clinical findings and a summary of the results of the tests are presented with each series of charts depicting the results of gastric contents analyses.

In eight cases the gastric acidity was within the accepted bounds of normality. In the sixteen other cases hyperacidity was present. In the first six cases presented the antacid properties of milk only were investigated; in all the others three antacid drugs were investigated in addition to milk, but about half way through the cases aluminium hydroxide was substituted for tribasic magnesium phosphate, and Sippy Powder No.2 (modified) for Sippy Powder No.1 (modified). Each antacid was actually investigated in the following number of cases in the manner set forth in Chapter III:-

Milk	.. .. .	.. .. .	24 cases
Magnesium trisilicate	.. .. .	.. .. .	18 cases
Sippy Powder No.1 (modified)	.. .. .	.. .. .	10 cases
Sippy Powder No.2 "	.. .. .	.. .. .	8 cases
Aluminium hydroxide	.. .. .	.. .. .	11 cases
Tribasic magnesium phosphate	.. .. .	.. .. .	7 cases

## CHAPTER V.

### The results of this investigation.

#### Discussion and conclusions.

The details regarding arrangement and technique, in these tests have already been discussed in Chapter III, and the results of the individual cases have been dealt with separately along with the case histories and charts. There only remains now the consideration of the investigation as a whole.

While the details of each case have been considered individually in coming finally to conclusions, one has now tried to collect the most important facts in the tables which follow, in an attempt to show the results as a whole.

Twenty four cases have been studied in the manner set forth in chapter III. Of these, six have received (for various reasons indicated) only the "control" test, in which the antacid (and also the acid-stimulant) effects of milk are demonstrated. At first 5 oz. milk feeds (as in Mann's investigation, 1937) were given (this applies also to cases 7 and 8) but it was feared that these would leave too small an amount of "free" acid in "the controls", and 3 oz. feeds were adopted. In the first six cases all degrees of acidity from "medium" normal to marked hyperacidity/



hyperacidity are shown. It is remarkable that so long as the acidity remains within the generally accepted "normal" limits during the gruel test meal, milk feeds (even reduced to 3 oz.) hourly are adequate either to control completely or almost abolish the "free" acidity throughout the test. So soon as the hyperacidity range is entered, however, at some points in the subsequent test the acid again becomes elevated to hyperacidity levels, i.e. above 40 units.

This interesting fact is also demonstrated in the remainder of the cases, - only a few of which of course fall within the "normal" range. As already mentioned, Dragstedt has shown that it is "free" acidities above 40 units which are dangerous to living tissues: (but one imagines that much lower acidities must also have a deleterious action on devitalised tissues, such as those in the region of a peptic ulcer). Hence the importance of the above observation, and the conclusion that milk feeds alone (even hourly) leave something to be desired when a peptic ulcer is under strict treatment. It seems probable that a hypersecretion as well as a hyperacidity is present in some of these cases, and this would account for the relatively great change in the effectiveness of milk observed in many (but not all) hyperacidity cases, as compared with those just within the normal range.

In the remaining 18 cases, four tests were  
carried out on each patient, three antacid drugs  
being investigated on each case.

In the first seven cases (Sippy Powder No.1  
(modified), magnesium trisilicate, and tribasic  
magnesium phosphate were given. During the first  
 part of the test when the effect of a single dose of  
 the drug was being tested, 20 grains of each were  
 given either immediately after or half an hour after  
 the meal, - these being the times and dosage usually  
 employed therapeutically. In the remainder of the  
 test, a dose of 20 grains was given hourly.

When these cases had been investigated, it was  
 decided that tribasic magnesium phosphate should be  
 discontinued since its effect was disappointing and  
 other remedies remained to be tried.

It appeared, too, that the 20 grain initial dose  
 had a transient effect in nearly all cases and all  
 drugs, and it was decided to try the effect of a  
 1 drachm dose without delay. Accordingly,  
 aluminium hydroxide was substituted for tribasic  
 magnesium phosphate in the remainder of the tests  
 (II), and the larger dose given.

In the next three tests the 20 grains dose in  
 the nine hour test remained the same, this bringing  
 the total up to ten for Sippy No.1 and magnesium  
 trisilicate.

In/



In the remaining eight tests, magnesium trisilicate and aluminium hydroxide were continued, Sippy Powder No.2 being substituted for No.1 and the doses in the nine-hour test becoming 40 grains instead of 20; the initial dose of 1 drachm was continued.

In the tables which follow the results of these investigations are epitomised. No definite effect of the drugs on motility was observed in these cases.

In table I, the effects of the initial 20 grain doses in the first seven cases mentioned above are shown.

In table II (a) the effects of the 20 grains hourly doses in the first ten cases described above are shown. (This represents the series in which magnesium trisilicate is compared with Sippy No.1, although tri-basic magnesium phosphate was discontinued at the seventh, and aluminium hydroxide substituted).

In table III the effects of the initial dose of 1 drachm are shown in the remaining eleven cases.

In table IV (a) the effects of hourly doses of grains 40 are shown in the last eight cases.

In table II (b) the total number of units of "free" hydrochloric acid recorded in the nine-hour test in each case for each antacid, and also the total for each antacid in the first ten cases are shown.

In table IV (b) results similar to table II (b) for the last eight cases are recorded.

The alteration in the initial dose, and the introduction of aluminium hydroxide for tribasic magnesium phosphate at the eighth case has caused some apparent confusion and difficulty in classifying the results, but the reasons for the change have been given, and the confusion and difficulty is therefore only apparent. Discussion of the results set forth in the tables follows them.



TABLE I.

THE EFFECTS OF A TWENTY GRAIN DOSE OF CERTAIN  
ANTACIDS ON THE ACIDITY RESPONSE TO A FRACT-  
TIONAL TEST MEAL.

DURATION OF TESTS. .... THREE HOURS.  
NUMBER OF CASES INVESTIGATED. SEVEN .  
ANTACIDS TESTED THUS... ... THREE .

I. SIPPY POWDER NO. I. (MODIFIED).

II. MAGNESIUM TRISILICATE. ("MAGSORBENT").

III. TRIBASIC MAGNESIUM PHOSPHATE.

<i>Duration of antacid effect.</i>	<i>Sippy Powder No. 1. gr. 20.</i>	<i>Magnesium Trisilicate, gr. 20.</i>	<i>Tribasic Magnesium Phosphate gr. 20.</i>
0 15 15 minutes.			
15 " 30 " .	4 cases.	2 cases.	5 cases.
30 " 45 " .	2 cases.		
45 " 60 " .		4 cases.	1 case.
60 " 75 " .	1 case.		1 case.
75 " 90 " .			
Over 90 " .		1 case.	
Presence of secondary acid-stimulant action.	6 cases.	2 cases	5 cases.
Presence of alkalinising action on stomach contents.	2 cases.	—	—
Powder preferred by patient (taste).	3 <sup>rd</sup> (7 cases)	1 <sup>st</sup> (7 cases.)	2 <sup>nd</sup> (7 cases.)
No. of cases.	7 cases.	7 cases	7 cases.



Discussion of the results shown in the above tables.

Table I.

The duration of the antacid effect and the other actions of a single dose of 20 grains of magnesium trisilicate, Sippy Powder No.1, and tribasic magnesium phosphate are shown in seven cases.

Magnesium trisilicate's antacid effect averaged 45 to 60 minutes, there was no alkalinising effect, and in only two cases out of seven was there any evidence of a secondary rise in "free" acidity following its antacid action. It was preferred by the patients in all cases.

Sippy No.1's effect lasted for little more than 30 minutes on the average, in two cases the stomach contents became distinctly alkaline with this small dose, and in six cases out of seven a secondary stimulation of acid secretion was produced. It was the least popular remedy with the patients in every case.

Tribasic magnesium phosphate's effect or the average was practically the same as that of Sippy Powder No.1, and in five cases out of seven a secondary acid stimulation was observed. It could not, of course, make the stomach contents alkaline, and was preferred to Sippy Powder on account of its less unpleasant taste.



Conclusions.

It appears then that in the small single infrequent doses so often employed therapeutically the administration of these remedies can scarcely be considered justified so far as the control of "free" acidity is concerned. This is especially the case with the Sippy Powder No.1 which has a short antacid effect (about 30 minutes) followed by acid secretion stimulation which appears to counter balance the short lived acid control. Moreover, it is unpleasant to take and may make the stomach contents alkaline. Tribasic magnesium phosphate's effect is equally transient and the secondary acid secretion almost as frequent. The other drawbacks are not, however, present.

Magnesium trisilicate's effect is usually more prolonged, (but this is only by 15 to 20 minutes at the most), it rarely gives rise to undesirable side effects, and is pleasant to take; it would therefore seem to be the best of these remedies. One cannot, however, believe that "free" acidity control of 45 minutes duration, three or four times a day would make any very real difference to the process of healing in a case of peptic ulceration, or that such treatment would be effective in preventing the development or recurrence of peptic ulceration, (for example after a course of strict medical treatment or after/

after gastro-enterostomy) if "free" acidity control were being relied upon to do this.

These powders, in small doses, especially if containing sodium bicarbonate, effectively relieve pain (for a time only) and hence their popularity with the patients, but they are poor palliatives, and lead the patient to neglect the more important aspects of treatment.

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TABLE II. (A).

## INVESTIGATION OF THE CONTROL OF "FREE" GASTRIC ACIDITY BY :-

I. MILK FEEDS HOURLY (USUALLY THREE OUNZES).

II. (I) WITH SIPPY NO. I. (GR. 20.) HOURLY BETWEEN FEEDS.

III. (I) WITH MAGNESIUM TRISILICATE (GR. 20.) HOURLY BETWEEN FEEDS.

IV. (I) WITH TRIBASIC MAGNESIUM PHOSPHATE (GR. 20.) HOURLY BETWEEN FEEDS.

V. (I) WITH ALUMINIUM HYDROXIDE (GR. 20.) HOURLY BETWEEN FEEDS.

(Note. Bracketed numbers indicate how often the acidity level indicated was reached in each case.)

Degree to which "free" acidity was controlled.	1. MILK feeds of 3oz. hourly + water 1oz. between the feeds.	2. MILK as in (1) + Sippy Powder No. 1, gr. 20 hourly in water 1oz.	3. MILK as in (1) + Magnesium Trisilicate gr. 20 hourly in water 1oz.	4. MILK as in (1) + Tribasic Magnesium Phosphate gr. 20. hourly in water 1oz.	5. MILK as in (1) + Alumini- um Hydrox- ide, gr. 20 hourly in water 1oz.
Complete control during the test.		X, X, X.	X, X, X.	X, X, X.	X.
"Free" acidity rising from time to time to between:- 0 and 10 units.			X (2).		
10 and 20 units.	X (4).	X (1), X (2).	X (3).	X (1).	X (1).
20 and 30 units.	X (3), X (3).		X (1), X (2).	X (2+).	X (2).
30 " 40 "	X (8).		X (1).		
40 " 50 "	<del>X (3)</del> , X (3).	X (1).	X (1)		
50 " 60 "	X (3).	X (1), X (1), X (1)			
60 " 70 "	X (1), X (2).		X (1).	X (1).	
70 " 80 "					
80 " 90 "	X (2).			X (1).	
90 " 100 "	X (1).	X (1).			
Alkalinising action on stomach contents.	—	X (1), X (1), X (1) X (1), X (2), X (2) X (3), X (4).	—	—	—
No. of bases.	10.	10.	10.	7.	3.



Table II.(A.)

The effect of hourly milk feeds on "free" acidity without and with antacids (grains 20) hourly between the feeds is shown.

It is shown that with milk feeds alone acidity rose to dangerously high levels (over 40 units, or between 30 and 40 for prolonged period) in all but three cases. (These three cases had a "normal" gruel test meal result).

With the addition of Sippy Powder No.1 control was satisfactory (maintained below 40 units) in five cases out of ten, and complete in three. An excessive alkalinising action was observed, however, in eight cases out of ten.

With the addition of magnesium trisilicate a satisfactory control was found in eight cases out of ten, with three completely controlled. No undesirable side effects observed. (This powder and aluminium hydroxide were most popular with the patients).

With the addition of tribasic magnesium phosphate a satisfactory result was achieved in five cases out of seven with complete control in three. No undesirable side effects. There were very poor results in two cases however.

With the addition of aluminium hydroxide (only three cases investigated with this dosage) control was satisfactory in all three and complete in one, with no side effects.



TABLE IV. (B).

(Tests as in Table IV. (A).).

INDICATES THE TOTAL NUMBER OF UNITS OF "FREE"

ACIDITY RECORDED IN THE EIGHT TESTS OF EACH

ANTACID MADE IN THIS PART OF THE INVESTIGATION.

Number of the case.	Total number of units of "free" hydrochloric acid recorded in each case in each test.			
	Milk feeds, (alone)	Milk feeds + Sippy 2 (gr. 40)	Milk feeds + Magnesium Trisilicate (gr. 40)	Milk feeds + Aluminum Hydroxide (gr. 40)
24.	337	0	0	10
20.	408	22	5	31
18.	413	30	82	0
22.	433	0	0	0
23.	582	64	2	0
19.	568	180	77	118
17.	225	108	47	69
21.	481	37	65	97
Total = 17 to 24.	3,447.	441.	278.	325.

TABLE II. (B).

INDICATES THE TOTAL NUMBER OF UNITS OF "FREE"

ACIDITY RECORDED IN THE VARYING NUMBER OF NINE

HOUR TESTS CARRIED OUT WITH EACH ANTACID.

(Tests as in Table II. (A).).

No. of case.	Total units of "free" hydrochloric acid recorded in nine-hour test in each case.				
	Milk feeds, (alone)	Milk feeds + Sippy I. (gr. 20.)	Milk feeds + Magnesium Trisilicate (gr. 20.)	Milk feeds + Tribasic Magnesium Phosphate (gr. 20.)	Milk feeds + Aluminum Hydroxide (gr. 20.)
7.	125.	2.	0.	0.	—
8.	68.	0.	0.	0.	—
9.	189.	29.	72.	0.	—
10.	326.	156.	59.	276.	—
11.	297.	32.	32.	24.	—
12.	452.	52.	14.	52 + 4 (incomplete)	—
13.	797.	548.	552.	710.	—
14.	233.	55.	73.	—	32.
15.	422.	125.	112.	—	64.
16.	639.	0.	0.	—	0.
Total = 7-16	3,541. (10 cases)	999. (10 cases)	914 (10 cases)	1,062 + (only 7 cases)	96 (3 cases.)



Table II. (B).

This shows the total number of units of "free" acidity recorded in each test in table II (A), and also the total for the series for each antacid.

Table II (A) indicates only the highest point reached (which is probably more important) in each test, this table shows how complete the control was throughout the other portions of the test.

A glance at this table shows how great a difference the additional frequent administration of antacids makes to acid control when compared with milk feeds alone. The totals indicate that, from this point of view, magnesium trisilicate was only slightly more effective than Sippy Powder No.1, but the great extremes of reaction produced by the latter must be remembered. Tribasic magnesium phosphates unsatisfactory result is shown, for more acid was present in seven cases with it, than with ten in the cases of the others.

Aluminium hydroxide is very effective in the three cases.

It will be noted that in case No.13 all the antacids studied, failed to control the acidity. This is attributed to great hypersecretion in addition to hyperacidity in this case.

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Conclusions.

It has been shown that milk feeds hourly without the addition of antacids between the feeds are insufficient in cases of hyperacidity to prevent the "free" acidity frequently reaching dangerous levels (i.e. over 40 units).

The addition of magnesium trisilicate (gr.20 between the feeds) achieves satisfactory control in nearly all cases without the production of any undesirable side action: Tribasic magnesium phosphate was much less effective, while Sippy Powder No.1 was effective in only half the cases, and also nearly always made the stomach contents alkaline from time to time, great extremes of reaction being recorded:

Aluminium hydroxide had an excellent effect in the three cases investigated.

It <sup>will be</sup> ~~has already been~~ pointed out, however, in discussing Table III, <sup>(A)</sup> that larger doses of neutral antacids (one drachm or more) with two hourly feeds would nearly always completely control acidity, and would be much less tiresome for the patient who should rest as much as possible.

It is therefore suggested that such frequent feeds and dosage as were employed in this section of the investigation and unnecessary and undesirable if the neutral antacids indicated be employed.

TABLE III.

THE EFFECTS OF A ONE DRACHM DOSE OF CERTAIN ANT-ACIDS ON THE ACIDITY RESPONSE TO A FRACTIONAL TEST MEAL.

DURATION OF TESTS. . . . . THREE HOURS.  
 NUMBER OF CASES INVESTIGATED. . . . . ELEVEN .  
 ANTACIDS TESTED THUS. . . . . FOUR .  
 I. SIPPY POWDER NO. I. (MODIFIED). . . . . THREE CASES.  
 II. SIPPY POWDER NO. II. " . . . . EIGHT CASES.  
 III. MAGNESIUM TRISILICATE. . . . . ELEVEN CASES.  
 IV. ALUMINIUM HYDROXIDE. . . . . ELEVEN CASES.

Duration of antacid effect.	Sippy Powder No. 1. 1 drachm.	Sippy Powder No. 2. 1 drachm.	Magnesium Trisilicate. 1 drachm.	Aluminium Hydroxide. 1 drachm.
0 to 30 minutes.	1 case.	1 case	2 cases.	2 cases.
30 " 60 "		5 cases.	3 cases.	1 case.
60 " 90 "		1 case		
90 " 120 "	1 case.	1 case.	4 cases	5 cases.
120 " 150 "	1 case.		2 cases.	2 cases.
150 " 180 "				1 case.
Presence of secondary acid stimulant action.	No cases.	4 cases.	5 cases.	1 case.
Presence of alkalinising action on stomach contents.	1 case	—	—	—
No. of cases.	3	8	11	11.



Table III.

The duration of the antacid effect and other actions of a single dose of one drachm of magnesium trisilicate (11 cases), aluminium hydroxide (11 cases), Sippy Powder No.2 (8 cases) and Sippy Powder No.1 (3 cases) are shown.

Magnesium trisilicate's antacid action averaged about 90 minutes, but with this larger dose a degree of secondary acid stimulation was observed in five cases out of eleven.

Aluminium hydroxide's antacid action averaged between 90 and 120 minutes and in only one case was a secondary acid stimulant action observed. Both this and the previous drug were preferred to the Sippy Powders on account of their tastelessness. An alkaline reaction was, of course, never observed in the stomach contents.

Sippy Powder's (No.2) antacid effect averaged somewhat less than 60 minutes (usually 30 minutes less than magnesium trisilicate) and in half the cases a secondary stimulation of acid secretion was present. With this powder, however, in contrast with the No.1 powder, an alkaline reaction was never observed in the stomach contents. ~~It was concluded therefore, that it is the magnesium oxide which is responsible for this undesirable effect.~~

Sippy/

Sippy Powder's No.1 (only three cases) appeared to have a more prolonged antacid action than No.2, but tended to alkalinise the stomach contents. No acid stimulant action observed in the three cases.

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### Conclusions.

One finds, therefore, that with doses of one drachm "free" acidity control may be expected to last from  $1\frac{1}{2}$  to 2 hours with aluminium hydroxide, without undesirable side effects, and for about  $1\frac{1}{2}$  hours with magnesium trisilicate where there is some tendency for more acid to be secreted afterwards. The antacid action with Sippy Powder No.2 is less satisfactory (somewhat less than 1 hour) and acid stimulation follows in half the cases, while the danger of alkalosis would have to be considered if such large doses of this powder were given frequently. (300 grains per day is considered the limit of safety).

It appears, therefore, that with two hourly feeds (e.g. milk 6 oz.) and one drachm of the above neutral antacids (preferably aluminium hydroxide) given 30 minutes after the feed practically complete control of "free" acidity could be confidently expected, without any danger of alkalosis, diarrhoea or other undesirable side effect. The powders of the Sippy type are obviously much less satisfactory. When the ulcer has healed and the period of strict acidity control is over, the advisability of continuing with one of those antacids three or four times daily must remain a matter of opinion; at least they will do no harm, but the writer, remembering especially the long period during the night when the stomachs of patients/

patients with hyperacidity contain acid of high concentration (Winkelstein, 1935, and Hellebrandt et alia, 1937) considers such therapy of doubtful value.

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The influence of hourly milk feeds (3oz.) (with and without the addition of hourly antacid drugs midway between feeds in doses of gr. 40.) on the acidity ("free") of the gastric contents.

Nine - hour test.

Eight cases investigated.

Antacids (in addition to milk feeds):-

1. Sippy Powders (modified) - No. 2.
2. Magnesium trisilicate.
3. Aluminium hydroxide.

A.

	1	2	3	4
Degree to which "free" acidity was controlled.	MILK. Milk feeds (3oz.) hourly + water 1oz. between the feeds.	MILK. as in (1) + Sippy Powder No. 2. gr. 40 in water 1oz. hourly.	MILK. as in (1). + Magnesium Trisilicate gr. 40 in water 1oz. hourly.	MILK. as in (1). + Aluminium Hydroxide gr. 40 in water 1oz. hourly.
Complete control throughout the test.		X, X.	X, X.	X, X, X.
"Free" acidity rising at times to :-				
0 to 10 units.		<del>X(1)</del> , <del>X(1)</del> .	X(1), X(1).	
10 to 20 "		<del>X(1)</del> .	X(1).	X(1), X(1).
20 to 30 "		X(1), X(1), X(1).		
30 to 40 "		X(2), X(1).	X(1), X(1).	X(1), X(1)
40 to 50 "	X(2), X(2).		X(1).	X(1).
50 to 60 "	X(3), X(1)	X(1).		
60 to 70 "	X(1), X(1), X(1).			
70 to 80 "	X(1).			
Excessive effect leading to alkalinity in stomach contents	—	—	—	—

Figures in brackets indicate the number of times the limit indicated was exceeded in the test.

Table IV.(A.).

This table is similar to II(A) except that Sippy Powder No.2. was given in place of No.I., aluminium hydroxide instead of tribasic magnesium phosphate, and dosage was increased to grains 40 hourly.

In every case the milk feeds alone were inadequate to keep the "free" acidity below 40 units.

With the addition of magnesium trisilicate between the feeds acid control was satisfactorily achieved in all but one case in which on one occasion only the "free" acidity rose to between 40 and 50 units. In two cases complete control was present, and no untoward effects were noted in any case.

With the addition of Sippy Powders No.2. an almost equally satisfactory result was obtained. Some degree of acidity was often present in those cases classed as "satisfactory," usually 10 to 20 units higher than in the magnesium trisilicate cases. Even with those very large doses the stomach contents never became alkaline as they frequently did with Sippy No.I.; ~~this effect must be due to the magnesium oxide content of the latter.~~

Aluminium hydroxide was similarly administered with a slightly better effect than magnesium trisilicate, complete control being achieved on three occasions, but 40 units "free" acidity again being exceeded in one case.



Table IV. (B.).

(Tests as for IV.(A.) and data as for II.(B).)

This table illustrates once more the inadequacy of the milk feeds alone in acid control, and the excellent action of all **three** antacids in the large doses employed. There was little to choose between them but the order of efficacy was magnesium trisilicate, aluminium hydroxide, Sippy Powder No.II.

NAME:  SSN:  DATE:  TIME:  SITE:  TIME:  NAME:  SSN:  DATE:  TIME:  SITE:  TIME:

### CONCLUSIONS.

Milk feeds (3 oz. hourly) are shown to be inadequate for "free" acid control in every case in this section, but the addition of 40 grain doses hourly of magnesium trisilicate, aluminium hydroxide and Sippy Powder No.2 are shown to be effective in controlling the acid in every case except one.

The first two are equally good and slightly better than the last, which, however, in this series, produced no excessive action in causing an alkaline reaction in the stomach contents. ~~This seems to be due to the absence of magnesium oxide which must have caused this effect in the Sippy No.1 cases in II (A).~~ Sippy No.2 powders in these large doses, however, have probably a tendency to cause constipation and alkalosis and the others would probably be better.

(A)

Evidence shown in Table III and explained in that section leads one to believe, however, that such large and frequent dosage is unnecessary when the neutral antacids above are used, and it was demonstrated there how two-hourly feeds with one drachm doses of aluminium hydroxide or magnesium trisilicate 30 minutes after the feeds would be sufficient to completely control "free" acidity in almost every case.



## SUMMARY OF THESIS

### SUMMARY OF CHAPTER I.

Notes on antacid remedies have been collected from medical literature throughout the ages beginning with the "Papyros Ebers" and continuing with references from the literature of the Greeks and Romans to the "dispensatories" of the sixteenth, seventeenth, and eighteenth centuries. The use of these remedies for "stomach troubles" can be traced (with the aid of a little imagination at times) from the earliest times right down to the present day.

It has been especially interesting to note that it is over a hundred years since the principle of controlling the bowels by means of variations in the antacids given for "heartburn" and allied conditions was first taught in the Edinburgh School, and almost as long since milk was first advocated as an antacid of the greatest importance.

### SUMMARY OF CHAPTER II.

#### THE ANTACIDS.

A review of the literature.

The experimental work on the effects of the antacids prior to the introduction of the fractional test meal/

meal is first discussed. The conflict of opinion towards the end of the nineteenth century is noted. Pawlow's important work on dogs was done about this time in which he demonstrated the satisfactory effect of sodium bicarbonate as an antacid.

The action of antacids in vitro is next considered and the writer's results tabulated. Most workers seem to be agreed as to the relative efficiency of the various remedies. Of neutral antacids, magnesium trisilicate was found to be good but less potent than the work of Mutch led one to expect. Tribasic magnesium phosphate was found by most investigators to be most potent, while aluminium hydroxide had a very poor effect in vitro. Amongst the "older" antacids magnesium oxide was found to be by far the most powerful and sodium bicarbonate, though much less effective, was much more powerful than the neutral antacids. Thus the Sippy Powders are more powerful in vitro than the newer remedies.

The experimental work since the introduction of the fractional test meal is next discussed. Crohn's work demonstrated the unsatisfactory effects of the "alkalis" with their excessive neutralising action followed by acid secretion stimulation. These results were confirmed by other workers and this led to the institution of a search for the "ideal" antacid.



antacid. Tribasic magnesium phosphate and allied drugs were advocated on theoretical grounds and were found to be satisfactory clinically by a few workers, but no very precise evidence of their efficacy was adduced and they were not generally adopted. Much work continued to be done on the older remedies, but little was added<sup>to</sup> the findings mentioned above: this work is reviewed critically. Meanwhile, many "ideal" antacids had been introduced and investigated mainly in America and on Continent, and these along with milk are reviewed separately.

The recent experimental work illustrating the excellent properties of milk as an antacid is noted.

Tribasic magnesium phosphate and related drugs are discussed. They were generally found to be very satisfactory but this opinion was based mainly on clinical impressions. It was therefore decided to include this drug in this investigation.

Aluminium hydroxide has been much investigated in America and on the Continent but little or no mention of it is made in British Literature. Its reported excellent effect in vivo belies the results universally found in vitro, but nevertheless almost all the evidence suggests that it is a good antacid. Ivy's careful investigation leads one to believe that it acts simply by virtue of its direct local neutralisation/

neutralisation of acidity, and seems to disprove many of the more extravagant suggestions which have been made regarding its effects. It was decided to include it in this investigation.

The silicates are next discussed. Aluminium silicate and calcium silicate have been frequently investigated on the Continent in the past ten years, usually with most satisfactory results, but it was in 1936 that Mutch introduced magnesium trisilicate to the profession, and demonstrated its excellent antacid potentialities in vitro. He included a few clinical experiments in his work, but these results were not so convincing. Mann (1937) investigated one case and showed its efficacy as an antacid in large doses. Since, therefore, the actions claimed for this remedy in vitro have not yet been investigated clinically it has been made the subject of special study in this work.

Finally a section is devoted to a review of some of the many recent researches which emphasise the importance of high "free" acidity in the stomach in the pathogenesis of peptic ulcer, and the present conflicting views of authorities on antacid therapy as set forth in the literature and standard text books is discussed. A consideration of the evidence so far available leads one to the conclusion that, in the early stages of peptic ulcer therapy at least, the antacids have a definite part to play.



SUMMARY OF CHAPTER III.This investigation.

An outline of the proposed investigation is first given indicating the nature and aims of the work. Each test consists of an analysis of the gastric contents over a period of twelve hours. During this time a gruel test meal (three hours), and hourly milk feeds (nine hours) are given. Cases are investigated on four occasions, and in the subsequent tests various antacids are given. The effect of a single dose of each remedy on the acid response to the test meal is first investigated, and then it is given hourly between milk feeds to observe its effect when given in a strict therapeutic régime. Thus four antacids are investigated in each case (including milk) and their effects are compared.

The details and rationale of the work are next discussed. The preparation for and control of the patient between the tests is described. Previous work of this nature is criticised briefly, and the steps taken in this work to avoid certain of the faults mentioned are indicated, and such fallacies as remain are noted.

Certain problems not fully dealt with in the preceeding section follow. The validity of the "control"/

"control" test, the consideration of the "normal" fractional test meal acid response, and the choice of the most suitable test meal are discussed. The value of the estimation of the total chlorides as an index to the acid secretory activity of the stomach is fully discussed, and the reasons given for its omission in this investigation. The choice of the antacids to be investigated is considered, and the chapter ends with a description of the arrangement of the case histories and charts which demonstrate all the results obtained in the investigation and form the next chapter.

#### SUMMARY OF CHAPTER IV.

The results of the analysis of gastric contents studied over several twelve hour periods in the same patient when varying antacid medication was in progress as described in Chapter III are presented.

Twenty four cases were thus investigated, and the clinical findings and a summary of the results of the tests are presented with each series of charts depicting the results of gastric contents analyses.

In eight cases the gastric acidity was within the accepted bounds of normality. In the sixteen other cases hyperacidity was present. In the first six/



six cases presented the antacid properties of milk only were investigated; in all the others three antacid drugs were investigated in addition to milk, but about half way through the cases aluminium hydroxide was substituted for tribasic magnesium phosphate, and Sippy Powder No.2 (modified) for Sippy Powder No.1 (modified). Each antacid was actually investigated in the following number of cases in the manner set forth in Chapter III:-

Milk .. .. .	24 cases
Magnesium trisilicate .. ..	18 cases
Sippy Powder No.1 (modified) ..	10 cases
Sippy Powder No.2 " .. ..	8 cases
Aluminium hydroxide .. ..	11 cases
Tribasic magnesium phosphate ..	7 cases

#### SUMMARY OF CHAPTER V.

##### A discussion of the results of this investigation.

The twenty four cases in which the antacid effects of milk were investigated are reviewed. The important observation was made that so long as the "free" acidity of the gastric contents remained within approximately "normal" limits in the ordinary gruel/

gruel test meal hourly milk feeds of three ounces were sufficient to control "free" acidity completely, or, at least, satisfactorily throughout the test. When, however, the hyperacidity range was entered it was found that during milk administration the "free" acidity always rose above the "dangerous" level of 40 units. (See Dragstedt, 1936).

Therefore, if one aims at adequate "free" acid control at least in the initial stages of treatment of a peptic ulcer (and modern research suggests that one should), then milk feeds alone, even when give as frequently as every hour, will not achieve this. It is realised, of course, that in the application of any antacid therapy the long period during the night, when high acid concentrations prevail in the stomach, has to be reckoned with, and it seems that control of acidity during this period will not be achieved short of employing a "continuous medicated milk drip" into the stomach, such as is advocated in America for cases resistant to the more usual forms of treatment. This last rather extravagant "refinement" of antacid therapy is not likely to find favour in this country. The fact remains that the great majority of cases eventually heal satisfactorily without much "free" acid control, but it has been shown that those where reasonable control has been attempted heal more quickly. If complete control can be achieved, for say/



say eighteen hours out of the twenty four by means of a simple régime, this line of treatment would be indicated in preference to one as a result of which little "free" acidity control could be expected. A method which, it is claimed, will accomplish this, is set forth below.

The control of "free" acidity following small doses (20 grains) of Sippy Powder No. I., magnesium trisilicate and tribasic magnesium phosphate is shown to be transient -- about 45 minutes with magnesium trisilicate and 30 minutes with the other two, both of which usually caused a secondary acid secretion stimulation which counter balanced their fleeting neutralising effect. It is suggested that, so far as acid control is concerned, the exhibition <sup>several times a day</sup> of these drugs (for example in an attempt to prevent the development or recurrence of a peptic ulcer, or for the temporary relief of symptoms in such a patient) is a procedure of little value. In so far as the powders will nearly always relieve symptoms for a short time their indiscriminate use may lead to neglect of the more important aspects of treatment -- general hygienic measures, a regular mode of life and carefully selected diet. Their use for the relief of pain and discomfort unaffected by other measures may become necessary from time to time, but adequate rest should be enjoined if a serious relapse or other developments are to be prevented.

These antacids were then given hourly (20 grains) between hourly milk feeds. Satisfactory acid control

was almost always achieved with magnesium trisilicate but tribasic magnesium phosphate was much less effective, while Sippy Powder No. I. failed to control the acidity in half the cases, but in the same cases frequently caused the stomach contents to become distinctly alkaline, great extremes of reaction being produced. In a further similar series of cases 40 grain doses were given with Sippy No. 2. in place of No. I. and aluminium hydroxide for tribasic magnesium phosphate. It was found that in this very large dosage all the antacids were very efficient in controlling the "free" acidity, the neutral antacids being only slightly better than Sippy No. 2. It is shown below that this very large and frequent dosage is unnecessary for adequate acid control. With this dosage of Sippy Powders alkalosis would become more than a remote possibility.

When the action of single doses of one drachm of the various remedies was studied it was found that magnesium trisilicate could nearly always be relied upon to control acidity almost completely for 90 minutes and aluminium hydroxide for slightly longer; the effect of Sippy No. 2. was about 30 minutes less but was not excessive while it lasted, as was that of Sippy No. I., due presumably to its content of magnesium oxide.

Thus, in applying these results to therapeutics, it is suggested that if one drachm of the neutral antacids, magnesium trisilicate or aluminium hydroxide were given 30 minutes after two hourly feeds throughout the day almost complete control of "free" acidity



would be assured for 18 hours out of 24 (allowing for  $7\frac{1}{2}$  hours sleep). This is a simple but effective antacid régime for the initial stages of peptic ulcer therapy compared with many at present advocated. The writer believes that more elaborate schemes of treatment, so far as acid control is concerned at least, are not required, and are contraindicated in so far as they interfere unduly with the patients mental and physical rest. The cost of these antacid remedies for the above treatment has been estimated at threepence and threepence halfpenny per day respectively for magnesium trisilicate and aluminium hydroxide.

The value of such remedies when given less frequently in large doses, as in the later stages of peptic ulcer therapy, is doubtful; if the general mode of life and dietetic habits of the patient are carefully regulated the remedies might form a useful adjunct to treatment if taken half to one hour after meals.

Sometimes there is a tendency for more acid to be secreted following magnesium trisilicate's antacid effect but this was practically absent with aluminium hydroxide, and no definite effect on the bowels or other secondary effects were observed with either remedy. When the effects of these remedies are compared with the older antacid mixtures, particularly if those contain magnesium oxide, there is no doubt that they constitute a significant therapeutic advance.

CONCLUSIONS.

- (1) Antacid remedies of some sort have been prescribed for indigestion since the dawn of medicine.
- (2) Whether the "neurogenic" theory or some other regarding the ultimate aetiology of peptic ulcer is correct, the most important single factor predisposing to its production and persistence would appear, from recent researches, to be an abnormally high concentration of "free" hydrochloric acid in the stomach.
- (3) In peptic ulcer therapy, during the healing stages at all events, adequate control of "free" acidity must be considered an important part of treatment.
- (4) In this investigation of the effects of antacids, hourly milk feeds were found to control acidity satisfactorily when the test meal showed this to fall within "normal" limits, but milk was quite inadequate for cases of hyperacidity.
- (5) The addition of hourly 20 grain doses of antacids between the feeds was found to exert excellent control in the cases of magnesium Trisilicate and aluminium hydroxide, but tribasic magnesium phosphate/



phosphate was much less successful, while Sippy Powder No.1 (modified) was satisfactory in only half the cases and frequently produced, in the same cases, ~~led to~~ a marked alkaline reaction in the stomach contents.

- (6) The addition of hourly 40 grain doses of the above antacids to the milk feeds (Sippy No.2 was used instead of Sippy No.1, and tribasic magnesium phosphate was not investigated) was quite efficient in all cases in controlling "free" acidity, but a real danger of alkalosis would be present with the alkaline remedies given in this dosage. Furthermore, such frequent feeds and doses are shown below to be unnecessary and undesirable.
- (7) The antacid effect of small single doses of the remedies (20 grains) was found never to exceed 45 minutes, and averaged 30 minutes for Sippy Powder No.1 and tribasic magnesium phosphate; the action of both of these remedies was counter balanced by the secondary acid stimulation they produced in the majority of cases. It is suggested, therefore, that exhibition of such doses several times a day (except for the temporary relief of symptoms) is valueless if not harmful.

(8)/

- (8) It was found that, following doses of one drachm, acid control could confidently be expected for one and a half hours with magnesium trisilicate and aluminium hydroxide, but for only one hour with Sippy Powder No.2 (no excessive effect was observed with the last, as was with No.1). Apart from some tendency to higher secretion following magnesium trisilicate, and the Sippy Powder, no untoward side effects were noted.
- (9) It is claimed therefore, that by giving one drachm of magnesium trisilicate, or, even better, aluminium hydroxide, thirty minutes after two hourly six ounce milk feeds, almost complete and certainly adequate control of acidity is assured for eighteen out of the twenty four hours. This is a simple safe scheme of antacid therapy for the initial stages of treatment of peptic ulceration which disturbs the patients' rest but little, and costs only threepence to threepence halfpenny per day.

Less frequent feeds and larger doses might possibly be equally effective, but this has not been investigated in this work.

- (10) The limitations of these drugs when given, even in large doses but infrequently in the later stages/



stages of therapy is emphasised, but they may be a useful adjunct to treatment on general hygienic and dietetic lines.

- (11) When, therefore, the effects of the neutral antacids, aluminium hydroxide and magnesium trisilicate, are compared with the older alkaline mixtures, there can be no doubt that despite the inevitable limitations of all local antacids, they constitute a significant therapeutic advance.
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